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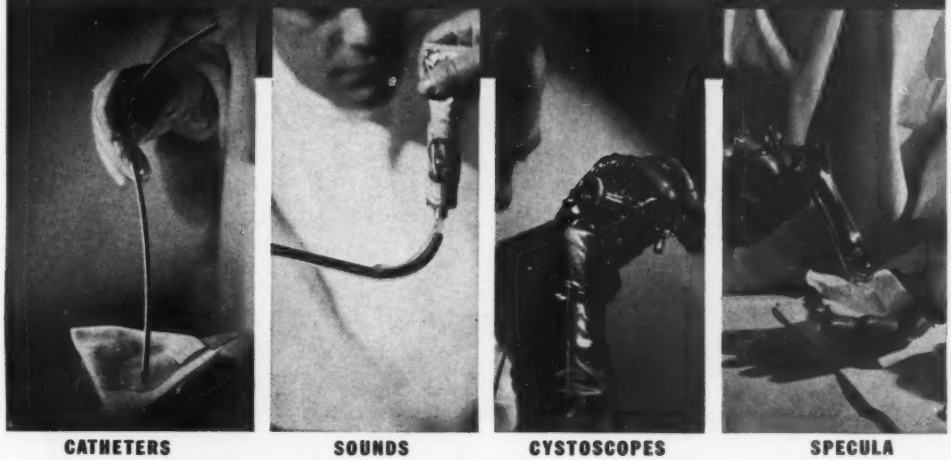

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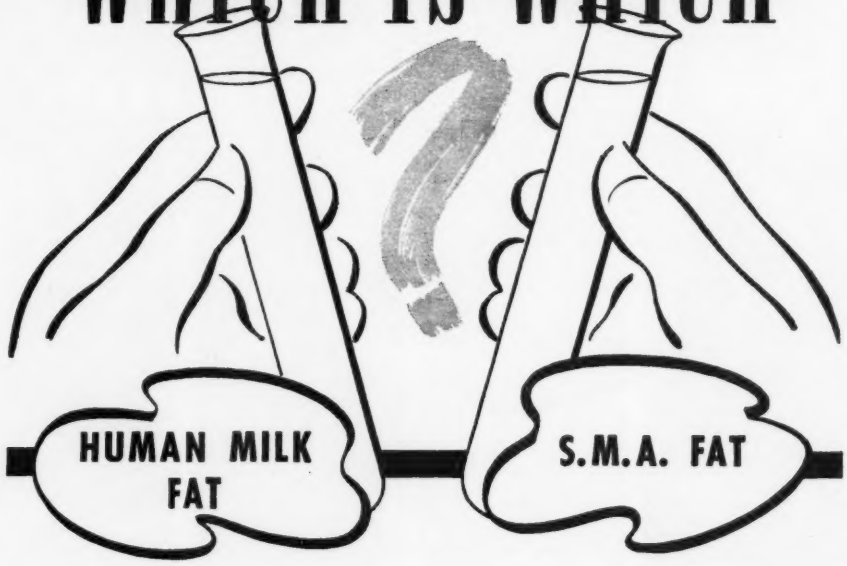

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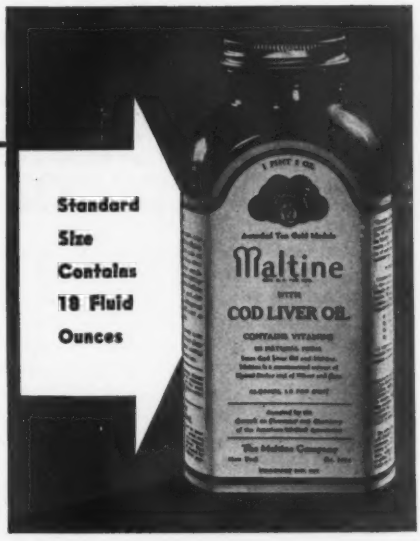

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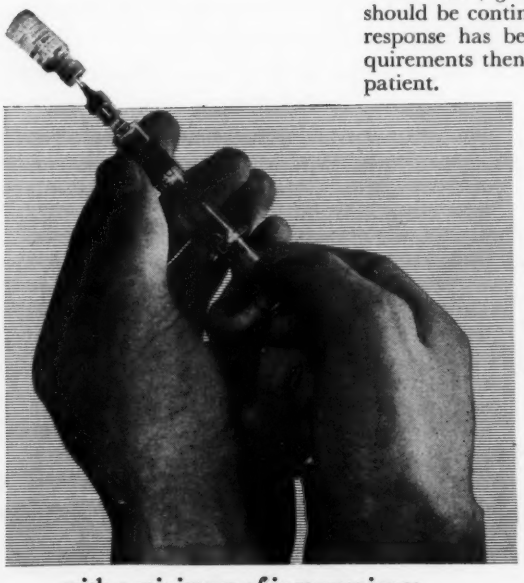

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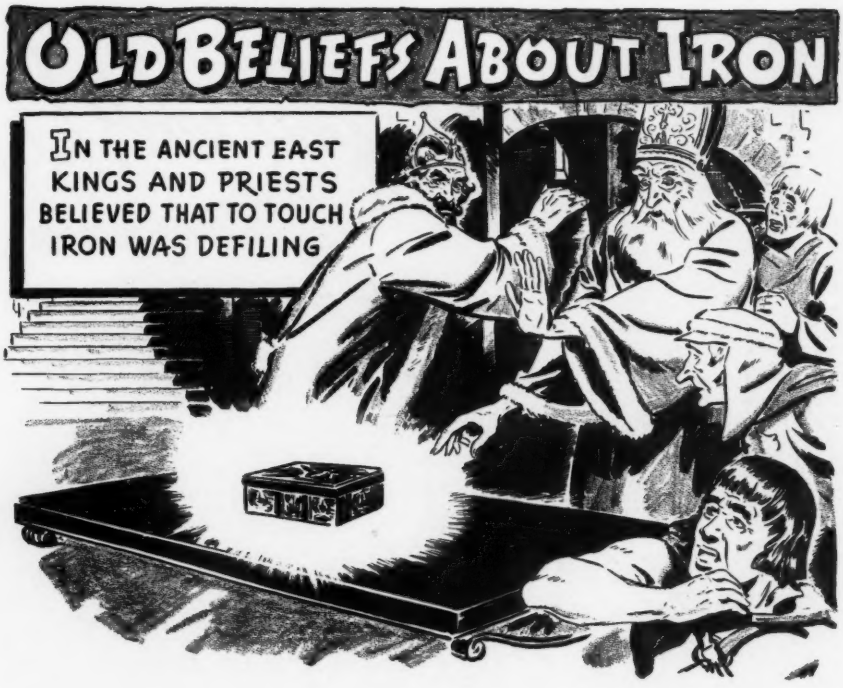

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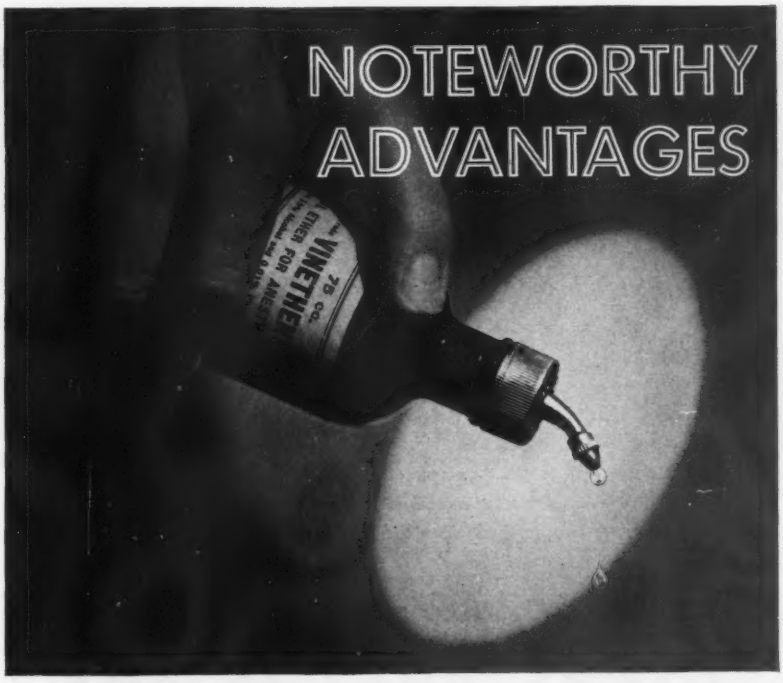

The factors which have led to the present usage of Vinethene in short operative procedures are its

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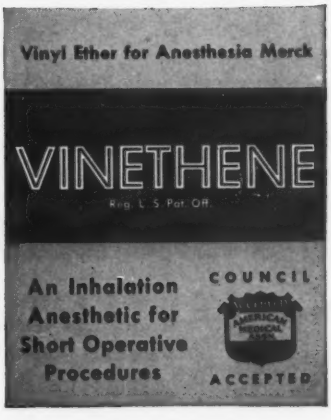

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Excellent for INTRAMUSCULAR *and Intravenous Injection*

It has been conclusively proved that the association of theophylline with a mercurial diuretic greatly enhances the local tolerance to the mercurial component. After intramuscular administration, the mercury component is absorbed more rapidly and completely from the site of injection, the rate of excretion is proportionately increased, and the diuretic effect is more prompt and more pronounced than when the mercurial alone is administered.

Salyrgan-Theophylline (10 per cent of Salyrgan* with 5 per cent of theophylline in solution) is absorbed quickly (97 per cent within an hour) and entirely from muscle tissue. As a result local soreness and pain are greatly reduced in intensity or not experienced at all.

Write for leaflet describing Salyrgan-Theophylline, including discussion of dosage, directions for use and contraindications and side effects.

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Salyrgan-Theophylline solution is supplied in ampules of 1 cc., boxes of 5 and 25; and ampules of 2 cc., boxes of 10 and 25.

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Of definite advantage in the management of chronic gall bladder and biliary tract disease is the induction of an increased flow of bile, flushing the entire biliary apparatus and thus removing pathogenic organisms and inflammatory products.

KETOCHOL . . . a combination of the oxidized or keto form of those BILE ACIDS (cholic, desoxycholic, chenodesoxycholic, and lithocholic) which are normally present in human bile—has been shown to stimulate an increased formation of aqueous bile, averaging 144%. Used in combination with frequent feedings of a diet rich in uncooked fats, and antispasmodic therapy, Ketochol offers a logical, clinically proved and highly effective means of treating chronic cholecystitis, cholangeitis, and certain cases of hepatic dysfunction and congestion.

Average dose: one tablet t.i.d. with or immediately after meals. *Supplied in bottles of 100 and 500 tablets.*

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ETHICAL PHARMACEUTICALS SINCE 1888

CHICAGO

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The August Southern Medical Journal the Vegex-Vitafood Dried Brewers' Yeast copy gave the biological assays (Albino rat) showing 50 International B_1 units and 40 Sherman-Bourquin units per gram of what is designated as B_2, and 5% in a vitamin B complex free diet—devoid of any of the B vitamins—gave normal growth over a period of eighteen weeks. These tests are for the whole, natural product without any additions of thiamin, riboflavin, nicotinic acid or other synthetic parts.

CLINICAL RESULTS—PELLAGRA

Goldberger and his associates were the first to publish the man test for dried brewers' yeast following the work of Goldberger, Waring and Tanner (Reprint No. 874 from the Public Health Reports) in which they state:

"The idea that pellagra is a communicable disease receives no support from this study.

"Pellagra may be completely prevented by diet."

As yet grain grown dried brewers' yeast is the most potent and complete known source of what Dr. Goldberger designated as the P-P (pellagra-preventive) factor.

From the clinical record, as reported from health officers and physicians throughout the pellagra sections, may be taken:

"We have had the most favorable results in this county from the use of your product. I am safe to say that at least seventy-five per cent of the patients that have taken this product, over the course of two or three months, have been cured and the other twenty-five per cent have been arrested, where it was taken any length of time.

"You will probably be interested to know that nearly fifty per cent of our insane cases, previous to the use of yeast, in our Health Work here, were suffering from pellagra. The number of insane cases from this cause is now practically nil."

Another health officer writes:

"I have treated over eight hundred cases (of pellagra) successfully by giving your yeast and a rigid diet."

REGULAR AND WIDE USE BY PHYSICIANS

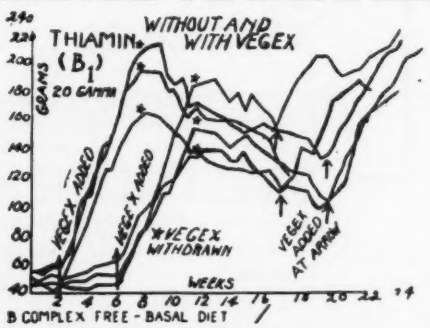
Out of almost five hundred replies to a questionnaire from physicians in the pellagra sections of the South, some 91% use Vegex-Vitafood Dried Brewers' Yeast in the treatment of pellagra and all report satisfactory results. The average amount for daily use is from one to three ounces. Along with the dried brewers' yeast fresh fruits, fresh vegetables, eggs, milk and butter are emphasized as well as all vitamins. The replies listed some sixty-six accompanying disorders.

VEGEX FOR THE PELLAGRA-PREVENTIVE FACTOR AND FULL VITAMIN B COMPLEX

Vegex, the condensed extract of autolyzed grain grown brewers' yeast, is among the pioneers for the full vitamin B complex in medical and nutritional research. It has now had the sixtieth published report showing aid in the treatment of the anemias; particularly for increasing the red blood cell count and hemoglobin percentage.

Mass man tests for pellagra have been had with Vegex with main use in Malay, Egypt, India, Roumania, Italy and the Southern States.

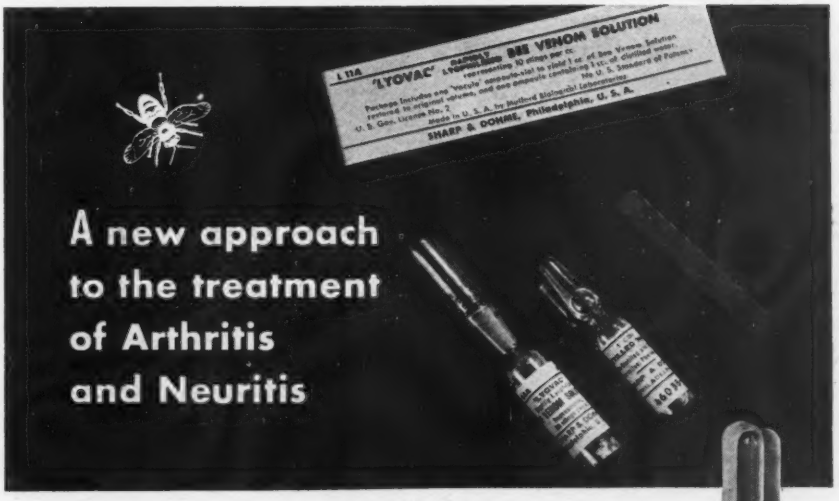
Thiamin (thiamin chloride) does not, alone, have the independent growth factor established for the B vitamins. In this test, after Vegex was withdrawn, the animals developed red inflammation around the ears, eyes and nose, loss of hair and dermatitis on jaws and paws, with dark, thick blood and increase up to 120% in hemoglobin. These conditions are showing relief with Vegex added back with the thiamin as shown in the chart.



Samples of Vegex and this Dried Brewers' Yeast in tablet or powder form, with special directions to physicians, will be sent on request.

VITAMIN FOOD CO., INC. **VEGEX, INCORPORATED**

122 Hudson Street, New York, N. Y.



'LYOVAC' BEE VENOM SOLUTION

SINCE the early days of history, bee venom has frequently been referred to in medical literature for its value in the treatment of arthritis and neuritis. The factors which kept it from widespread use have now been overcome in 'Lyovac' Bee Venom Solution, which supplies standardized bee venom in a stable form which retains its potency for many years.

Published reports[1, 2] of the effectiveness of Mulford 'Lyovac' Bee Venom Solution in reducing swelling, relieving pain and improving joint motility are paralleled by similar reports from physicians in general practice. It is indicated in the treatment of acute and chronic arthritis. It appears to be most effective in extra-articular manifestations, such as muscular rheumatism, sciatica, lumbago, neuritis, and iritis.

Mulford 'Lyovac' Bee Venom Solution is packaged under the new lyophile process by which the original therapeutic value of freshly prepared biological substances at the time of their highest potency is retained for many years.

Specify **'LYOVAC' BIOLOGICALS**

Mulford 'Lyovac' Bee Venom Solution represents the whole venom of ten bee stings. After candle filtration, for sterility, the solution is rapidly frozen and rapidly dehydrated under high vacuum. It is preserved under vacuum in the specially-devised 'Vacule' flame-sealed ampoule-vial.

Detailed information on the use of this product, the dosage schedule and method of application will be sent on request.

1. South. Med. & Surg., 100:555, Nov., '38
2. Nebraska M. J., 24:298, Aug., '39

"For the Conservation of Life"

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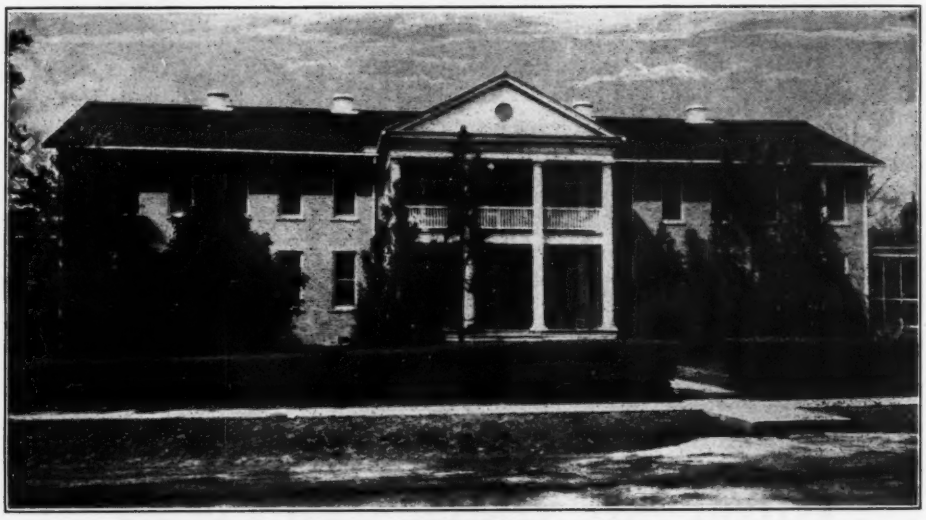

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The Tucker Sanatorium is for the treatment of nervous and endocrine diseases. There are departments of massage, medicinal exercises, hydrotherapy and physiotherapy. The Sanatorium is large and bright, surrounded by a lawn and shady walks, large verandas and has a roof garden. It is situated in the best part of Richmond and is thoroughly and modernly equipped. The nurses are specially trained in the care of nervous cases.

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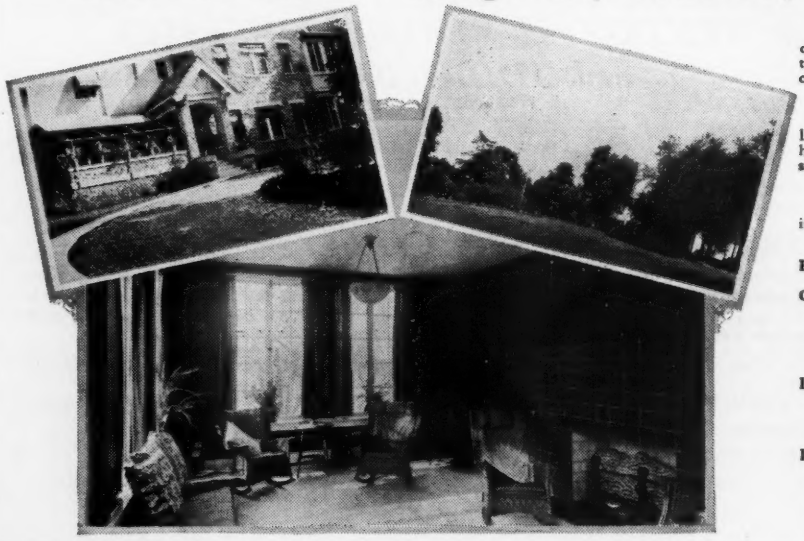

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References: Medical profession of Birmingham and Birmingham Chamber of Commerce.

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JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION

PUBLISHED MONTHLY BY THE SOUTHERN MEDICAL ASSOCIATION AT BIRMINGHAM, ALA.

Volume 32 OCTOBER 1939 Number 10

'FORCE FLUIDS': AN EVALUATION OF AND INDICATIONS FOR FLUIDS IN DISEASE*

By VIRGIL E. SIMPSON, B.S., M.D., F.A.C.P.
Louisville, Kentucky

In health the human body seems to be adequately provided against the likelihood of water intoxication. The sick individual may have some of the factors of safety impaired and is helpless to a considerable extent as to the control of water intake because the physician of today resorts frequently to intravenous introduction. Too much water in health will produce symptoms of water intoxication and death is possible. The same condition can obtain in disease, and it is this conviction that has prompted this discussion.

WATER CONTENT IN THE BODY

About 60 per cent of the total human body and 80 per cent of the soft tissues is water. Any increase of water in cells or tissue above this 80 per cent permits the designation of edema. That the percentage of water held by the normal cell is rather constant over long periods is evidenced by the minimal variation in weight of an individual. Instead of saying that we maintain a constant weight we might say, chemically, that we have maintained a constant degree of hydration of the tissues.

Water found in the cell is chemically bound to its colloid. While the water in the blood is maintained at a rather constant level, that in the lymph is extremely variable, and as Elwyn[1] emphasizes, it depends somewhat upon the activity of the organs from which it comes. Increasing the activity of an organ increases the amount of lymph. The water which is not bound to the colloids is called free water and varies considerably in amount, even from hour to hour. Water found in the organism is in a constant state of motion, being lost from the blood stream through excretion from the kidney, lung, skin and the digestive tract. The water thus lost is made up from the free water in the tissues. Reaching the blood stream from the alimentary tract, a series of changes is inaugurated by a movement of salt to establish an isotonic solution. One of these changes is a diminution of concentration of hemoglobin, requiring some forty-five hours for the fasting values to be reached.

Thirst, one of the protective mechanisms, is a more dependable guide as to the need of fluid than is appetite as to the need of food. It is largely the result of diminished secretion and drying of the nerve endings on the back of the tongue. The thirst experienced after an operation is not wholly the result of dehydration, but partly the action of atropine often administered by the anesthetist to diminish vagal inhibition.

After the ingestion of water, diuresis begins in fifty or sixty minutes and continues for two or three hours. Some of the water leaving the blood stream goes into storage in muscles, skin and liver. The function of these depots is to take up excess water, returning it as needed to the blood stream.

REGULATION OF WATER EXCHANGE

With a steady continuous loss of water from the blood there must be a comparative inflow from the water depots and keeping this rate of flow at a constant value implies a regulatory mechanism (McDowell[2]). This is accomplished by: (a) a peripheral, physicochemical system that determines the permeability of membranes, depending upon the electrolytic content of water on both sides; (b) a central nervous system control by the hypothalamus; and (c) hormonal regulation.

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These factors permit of further elucidation. The peripheral physicochemical regulation of water movement in the body depends on the concentration of electrolytes in the protoplasm, chief of which are calcium, sodium, potassium and hydrogen. The rate of water movement depends upon the electrolytic content of the water and the ability of the individual cell to take it up. Investigations into this function of the hypothalamus indicate that from it impulses originate that increase or diminish the rate of water movement.

The hormone regulation of water movement comes from the thyroid and the posterior lobe of the hypophysis. The thyroid hormone accelerates water movement. This is probably due to the increase in metabolic rate and its effect on the membranes through which the water moves. The pituitary is in close relation to the hypothalamus and there is, perhaps, some reciprocal influence between them. The hormone of the posterior lobe slows the rate of water movement through tissues probably by its action on the physicochemical mechanism.

WHAT CONSTITUTES EXCESSIVE WATER INTAKE?

If, after some surgical procedure, the patient takes an excessive amount of fluid, he will be unduly disturbed by the necessity of getting rid of it. This has obvious disadvantages when quiet is essential, as after hemorrhage. But more important than this, excessive intake may result in retention of fluid, local or general. This fluid infiltrates the tissues or accumulates in serous cavities. The plasma is diluted in consequence, protein loss becomes a factor and the mechanism by which fluid is retained in the blood vessels may be upset. Normally, on the one hand a capillary blood pressure tends to drive fluid out of the vessels, while on the other the osmotic pressure of plasma protein prevents its leaving. Infiltration of tissues may thus result from an increased capillary pressure, matching the consequences of venous back pressure or the increased permeability of capillaries that permits the passage of protein. Fischer[3] thinks increased permeability of capillary walls is imaginary and insists that edema is the result of chemical changes in the cells, the consequence of defective circulation. The retention of fluid in low-grade nephritis is easier for the clinician to understand. Such fluid begins to accumulate in parts of the body where the subcutaneous tissue is loose and where circulation is less efficient.

In such conditions, particularly following operative procedures, circulatory stasis and high venous pressure lurk in the background. Circulation of venous blood depends upon a variety of factors: the heart, the veins, the respiration and arterial pressure, and failure of any of these may make recovery impossible. The routine procedure of throwing a large quantity of fluid abruptly into the vascular tree puts a demand upon the heart concerning which the physician or surgeon admittedly knows too little. Under such a load one of two things may happen: the heart will cease beating or will dilate and evacuate its contents back into the veins instead of propelling them into the arteries. Such a dilatation results in valvular incompetency and strain behind. The cardiac reserve too long exceeded spells acute heart failure, and death may result.

Laboratory workers have conducted experiments on themselves and volunteer subjects to determine how much water may be drunk in a limited time and how much the kidney may eliminate. MacCullom and Benson's experiments show that as much as 2,500 c. c. of water can be taken in two hours and the output of urine reach a maximum of 20 c. c. per minute. Priestley[4] experimented on himself and found that he could drink two liters of water in fifteen minutes. In another experiment he drank 5,500 c. c. of water in six hours and voided 5,460 c. c. of urine, a rate of excretion of 1,200 c. c. per hour.

Experiments in diseased individuals have proven equally interesting. Many clinicians have observed that in typhoid fever as much as ten liters of water per day have been taken and no apparent ill effects noted. Drinking enormous quantities of water has been reported in patients with diabetes insipidus. Trousseau reported a case in 1867 that still stands as the highest rate of water exchange on record. His patient drank 40 liters per day, with a urinary output of 43, without symptoms of water intoxication. The conclusion reached in reading such reports is that neither the quantity of water that is drunk nor the rate of water exchange constitutes the risk, but that whenever the intake is in excess of the ability of the body to eliminate, the water balance is upset and symptoms of water intoxication result (Weir, Larson and Rowntree[5]). As a result of his studies, Rowntree[6] reached the following conclusions: (1) that water taken in excess of ability to excrete it leads to water intoxication; (2) that water in-

toxication will kill unless the excessive intake is stopped; (3) the rapidity of the advent of death varies; (4) water intoxication is usually accompanied by and probably is largely due to an increase in intracranial pressure; (5) many of the symptoms are manifestations of disturbance of the salt and water equilibrium; (6) excessive intake of water results in dilution of the blood, as shown by the decreased hemoglobin, serum protein, viscosity, the electrical conduction and the molecular concentration; (7) the symptoms of water intoxication are restlessness, asthenia, polyuria, diarrhea, salivation, retching, vomiting, tremor, twitching, convulsions, spasm, stupor and coma, with at times oliguria; (8) the convulsions are general in nature; (9) water intoxication can be prevented, alleviated or even cured by the administration intravenously of a hypertonic solution of sodium chloride.

In relation to edema two questions present themselves: (1) is there a greater amount of water in the tissues than normal, and (2) why does the water not move at a more rapid rate toward the blood stream? The chief difficulty in edema is in the rate with which the water movement is carried on. In edema there is maintenance of the regulation of water movement, though the blood volume remains nearly normal, the difference being that it is effected at a different level of activity, hence there is a slowing in the rate of water movement. Whenever the flow of blood through the glomeruli is slowed there results a threatened increase in the volume of the water content of the blood. This is a characteristic picture in the congested kidney of circulatory stasis. Elwyn[1] says that if the amount of water retained approaches five liters, it becomes distinctly visible as edema.

The regulatory centers can become affected so as to depress the function of the whole mechanism for water regulation. Along with this depression the other vegetative functions correspondingly sink to lower levels. This happens, periodically, in a hibernating animal, and in such conditions as myxedema, undernutrition, diabetes with edema, there is a diminution in the tempo of the vegetative functions of the body.

There are certain fundamentals in the treatment of a developing edema that cannot be sacrificed. (a) The intake of water must be held below that of the output, no matter how small the output may be. (b) The elimination of sodium chloride becomes a practical necessity. (c) The rate of oxidative processes in the cell must be maintained near normal. Many popular diets, for example, Karrell's, are basically wrong. They contain too much fluid and salt. The intake of water for an adult may be reduced as low as 300 c. c. per day. This, with a low salt intake, can be maintained for several days without difficulty. Acceleration of the rate of oxidative processes in the cells is more difficult to attain. It can be accomplished by food, particularly protein, since protein increases the metabolic rate because of its specific dynamic action. As long as there is no retention of nitrogenous end products, it is a safe procedure, and besides, urea may serve as a diuretic. A second means of increasing the oxidative processes is the administration of thyroid, but its dose must be adequate. Its beneficial effects were stressed by Eppinger as long ago as 1917 and emphasized by Epstein.[7] If, because of edema, thyroid is not absorbed from the alimentary tract, thyroxin intravenously should be given in doses of a tenth of a grain at five-day intervals.

RENAL INSUFFICIENCY

One may think of renal insufficiency in the same sense as one would think of myocardial or liver insufficiency. The maximum amount of water that a kidney can excrete continuously has never been determined. Krischne estimated it at about a liter an hour. In diabetes insipidus 10 to 12 liters may be eliminated each 24 hours. It might be said that 500 c. c. per hour is within the normal capacity of a healthy kidney. Richards[8] showed the process of water elimination in the glomeruli to be one of filtration and not of secretion. Each glomerulus is covered with an enormous capillary surface and the ability to vary the number of active glomeruli and of active capillaries in a single glomerulus explains the ability of the kidneys to adapt themselves to all changes that affect water content of the body. Relative renal insufficiency may be said to be dependent upon exclusion of a certain number of glomeruli and tubules from the functioning part of the kidney. As this is reduced the elimination time of water excess becomes longer and the ability to concentrate, as measured by specific gravity, becomes less. Just how much kidney substance could be lost and function preserved able to excrete the waste products from protein metabolism and water from the blood cannot be answered. The factor of safety varies with each individual kidney.

Christian[9] says that experimentally as much as 66 per cent of the kidney substance may be removed without loss of ability to excrete all of the waste products from the blood.

ACID-BASE EQUILIBRIUM

Edema results most frequently from impaired circulation. One of the functions of the blood is to carry such waste products as carbon dioxide, and in edema it increases above its physiologic level to be carried as carbonic acid. Laboratory studies show that hydrophilic properties of excised organs and colloids are increased by tissue acid accumulation. The deduction is that stagnant blood, improperly oxygenated, with tissue acid results in increased hydration capacity of tissues. Mason and Hellbaum[10] studied the influence of bicarbonate of soda on this phase of hydration and reported that 36 grams of the drug given patients over a period of three days produced a 90 per cent increase in weight. The average increase in weight gain was 2.2 pounds per subject. They concluded that this influence of alkalis increased kidney function chiefly through the dissolution of casts. On the other hand, sodium chloride decreased the alkaline reserve as determined by the carbon dioxide combining power of blood plasma, and this in turn induced diuresis. The effects were much like those of hyperpnea. In their clinical experiments they found that the administration of 7.5 grains of ammonium chloride daily resulted in a loss of weight from 0.5 to 3.7 pounds and effected a reduction in the hydrogen ion concentration amounting to about one-half its increase from sodium bicarbonate.

The blood volume is not materially affected by the ingestion of ordinary quantities of water. The rapid distribution of fluid or its excretion does not appear to be essential so much from the viewpoint of the maintenance of blood volume, as it is a necessity for the preservation of osmotic equilibrium. Greene and Rowntree[11] showed that while the administration of excessive amounts of water to dogs would result in convulsions, these symptoms did not occur if an isotonic saline were used, and that when these symptoms were produced by the introduction of excessive amounts of water, they could be almost immediately cleared up by the use of hypertonic salt solutions. Smith and Mendel[12] found that they could inject an isotonic solution of various neutral sodium salts in amounts that would double the blood volume, and that while these different salts were eliminated from the blood at various rates of rapidity, most of the fluid had passed into the tissues within five minutes after its injection without evidence of edema.

A somewhat different effect is noticed when nonelectrolytes such as glucose and urea are administered. The diabetic patient who has a persistent hyperglycemia without glycosuria will have a normal blood and plasma volume. If, however, glycosuria results, either because of diabetes or the injection of large amounts of glucose, diuresis with dehydration and profound anhydremia follow. Urea differs from glucose in that it cannot be destroyed in the body, and when given in sufficient doses it will produce diuresis and anhydremia. When using electrolyte solutions one is dealing with substances freely permeable through vessel walls. Quite different is the reaction to solutions of colloid, as these substances cannot traverse the body membranes, or do so with great difficulty, and if introduced directly into the blood stream, they increase the volume of circulating blood. They have, therefore, been extensively used to restore blood pressure and volume in shock and hemorrhage.

Underhill and Sallick[13] demonstrated that dogs given water equal to as much as two-thirds of their weight suffer from a reduction of from 10 to 15 per cent in their hemoglobin and as much as 25 to 35 per cent in the chloride concentration of the whole blood. The toxic effects of taking large amounts of water do not occur if salt is freely given. From this it would appear that these effects are due rather to the diminution in the electrolyte content of the cellular fluids than to the actual increase in volume.

Notwithstanding the fact that the components on the acid side show great variation, the total concentration of acid must remain quite as constant as that of the base, otherwise an equilibrium could not be maintained. Bicarbonates are the most easily eliminated and hence in emergencies rapid elimination of the carbonates or carbonic acid must take place. Carbonic acid is a weak acid and is an excellent buffer. Being volatile, it can be excreted by the lungs. The bicarbonates are spoken of as the alkali reserve of the body and are really the most useful single ions in the maintenance of an acid-base equilibrium in the blood. Whenever there is a reduction of blood bicarbonates, the condition is spoken of as an acidosis. Under usual circumstances respiration is so regulated that the excretion of carbon dioxide keeps pace with its

production, and hence the ratio of carbonic acid to bicarbonates is relatively constant. If the respiratory mechanism fails quantitatively, the pH of the blood falls.

The respiratory system and bicarbonates are usually sufficient to combat acidosis, at least as a temporary expedient. The ultimate adjustment of an acid-base electrolytic pattern of the blood and tissues must be maintained by the kidney. One of the most important substances eliminated by the kidney is ammonia, formed in the kidney from the neutral compound urea. Its production and excretion are regulated in accordance with the needs of the body from the standpoint of conservation of mineral base. Other things being equal, edema comes and goes according to the concentration of albumin in the serum. This is but another way of saying that edema comes and goes according to the colloid osmotic pressure, which depends chiefly upon the concentration of the albumin. It may be somewhat of a new thought to say that the kidneys are not to be blamed for edema as a rule except so far as they participate in the reduction of the albumin by leakage into the urine. Sodium chloride almost always increases edema; a salt-poor diet has a tendency toward a diuretic action and lessens edema. Potassium salts are much less likely to cause water retention and they may even induce diuresis. There are at least two chemicals that are definitely concerned with the retention of fluid, bicarbonate of soda and sodium chloride, and on the other side are the acidifying chlorides, such as ammonium and calcium, that have some diuretic effect. The above statement with regard to these chemicals may be termed somewhat of a theory when viewed in the light of what is called the serum electrolyte picture, and yet this picture is not much clearer as an explanation of anomalous conditions. The most common electrolytic abnormality is serum calcium deficiency, the fraction of calcium that is combined with protein constituting the deficiency.

The acidosis of uremia depends upon the reduction of bicarbonate. It is the inability to form ammonia that compels the nephritic to utilize mineral bases for neutralization of urinary acid. Another factor of importance in the acidosis of the nephritic is the increase of serum phosphate. It has been generally thought that phosphate accumulates in the serum because the kidney cannot excrete the phosphoric acid ion. This is probably an error, but a more satisfactory explanation has not yet been offered. A high serum sulphate also contributes to the acidosis of nephritics. It has been thought that its increase is due to retention or rather the failure of the kidney to eliminate the sulphates. The treatment of this condition is not within the scope of this paper except insofar as it does lend importance to the thought herein presented that the vigorous use of fluid following operative procedures, etc., is not a sound therapeutic procedure. The management consists fundamentally in the restriction of sodium chloride, the administration of adequate amounts of protein, the giving of sodium bicarbonate to allay the dyspnea and the use of diets that yield an alkaline ash. There is no place in such a regimen for the hackneyed phrase, "Force fluids."

The acid-base equilibrium is of relatively little importance in the ordinary congestive failure of the heart, but if there is a kidney deficiency, then the acid-base ratios become of extreme importance. The inorganic elements of the body are not equally and evenly distributed throughout the various media. In the human blood, for example, potassium is found chiefly in the cells, while sodium and calcium are confined almost entirely to the serum, and on the other hand magnesium is rather evenly distributed between the two. According to Peters and Van Slyke,[14] there is some 50 per cent more bicarbonate in the serum than there is in the blood cells, and as much as 100 per cent more chlorides in the serum than is found in the cells. Inorganic phosphate, on the other hand, is fairly evenly distributed between the two, but as emphasized by McDowell,[2] while playing an important part in buffering, it does not leave the cells except when in excess. The permeability of cell membranes to these substances is also of some importance in the maintenance of an acid-base equilibrium. Bicarbonate is the only electrolyte which can penetrate the cell membranes readily. This is one of the broad provisions of nature because carbon dioxide, which is produced by metabolic changes throughout the entire body, must escape from the tissues and the easiest method is through combination as a bicarbonate. Foods contain but little sodium, and our chief source of this element is in the form of table salt, while potassium, on the other hand, is found in many foods. Consequently it is relatively easy to prepare a diet that contains little sodium, but a comparably difficult one to prepare a diet that restricts potassium. One of the dangers of disturbing

osmotic pressure as a consequence of upsetting an acid-base equilibrium is found in the phenomenon of water intoxication. When large amounts of water are taken, salt is retained until the excessive fluid is eliminated. If the kidney is unable to eliminate the fluid, then edema must take place. If water can be eliminated from the body, salt which has dissolved in it will also be lost.

In normal blood serum 90 per cent of the base is composed of sodium, two-thirds of the acid is made up of chlorides, while one-fifth is bicarbonate and about one-tenth is protein. Protein acts as an acid and can combine, therefore, with a certain quantity of base. The variation in the concentration of the total base in the body is remarkably constant, while on the acid side the individual components show great variation.

CONCLUSIONS

Water, a necessity and sometimes an urgent one, may be as harmful as it may be helpful.

Routine procedures may be as subversive as routine thinking.

To write an order to have fluids forced may be as unnecessary as to order a heart digitalized because, forsooth, it has a defective valve.

To force fluids on a patient with prostatism soon to have some surgical procedure done may be as full of therapeutic wisdom as to order an anesthetic for a patient suffering from insomnia.

The method resorted to in forcing fluid may prove the deciding factor for harm. If the patient is asked to drink it, nature's safeguards are permitted to operate, but surgeons have come to act as if salvation could be achieved only intravenously.

The factor of safety against water poisoning is admittedly great because nature has so abundantly provided against water intoxication; diarrhea, diuresis, perspiration, the sense of satiety, contraction of the pylorus, all combine to safeguard against this factor. These protective mechanisms act during health, but may not if the sick patient is subjected to the indiscriminate administration of water.

One might paraphrase a great surgeon by concluding, "Force fluids," if you must; "force fluids" intravenously, if you dare!

BIBLIOGRAPHY

1. Elwyn, Herman: Nephritis. Cyclopedia of Medicine, **7**:763. Philadelphia: F. A. Davis Co., 1933.
2. McDowell, R. J. S.: Clinical Physiology. New York: D. Appleton & Co., 1927.
3. Fischer, Martin: Edema. Cyclopedia of Medicine, **5**:1. Philadelphia: F. A. Davis Co., 1933.
4. Priestley, J. G.: The Regulation of Excretion of Water by the Kidneys. Jour. Physiol., **50**:304, 1916.
5. Weir, J. F.; Larson, E. E.; and Rowntree, L. G.: Studies in Diabetes Insipidus, Water Balance and Water Intoxication. Arch. Int. Med., **29**:306 (March) 1922.
6. Rowntree, L. G.: Water Intoxication. Arch. Int. Med., **32**: 157 (Aug.) 1923.
   Ibid.: The Effects on Mammals of the Administration of Excessive Quantities of Water. Jour. Pharm. Exper. Therap., **29**:135, 1926.
7. Epstein: Nephritis. J.A.M.A., **87**:913 (Sept. 18) 1926.
8. Richards, A. N.: Kidney Function. Amer. Jour. Med. Sci., **163**:1 (Jan.) 1922.
9. Christian, H. A.: A Glomerular Dominance in Bright's Disease. Jour. Amer. Med. Sci., **96**:761 (Dec.) 1938.
10. Mason, C.; and Hellbaum, A. A.: Acid-Base Water Balance. Ann. Int. Med., **11**:2206 (June) 1938.
11. Greene, C. H.; and Rowntree, L. G.: The Effect of Experimental Administration of Excessive Amounts of Water on Volume and Concentration of the Blood. Amer. Jour. Physiol., **80**:209, 1927.
12. Smith, A. H.; and Mendel, L. B.: The Adjustment of Blood Volume After Injections of Isotonic Solutions of Varied Composition. Amer. Jour. Physiol., **71**:395, 1924-25.
13. Underhill, F. P.; and Sallick, M. A.: On the Mechanism of Water Intoxication. Jour. Biol. Chem., **63**:61, 1925.
14. Peters, J. P.; and Van Slyke, D. D.: Quantitative Clinical Chemistry. Baltimore: Williams & Wilkins Company, 1931.

DISCUSSION (*Abstract*)

Dr. C. W. Dowden, Louisville, Ky.—I desire to stress the point that Dr. Simpson is not recommending the restriction of fluids, nor denying the value of forcing fluids, when they are indicated. Concerning water balance, much has been established on a basis of sound physiologic facts, but application of these facts to the clinical treatment of disease remains many times in the field of conjecture. Dr. Simpson has described the fate of water after it enters the system; the manner in which it is distributed to the cells of tissues and organs of the body; how it is lost and then replaced. He has explained the factors concerned in this movement. Hydrostatic pressure in capillaries, the effective osmotic pressure of the blood plasma, the tension pressure of the tissue cells and the effective osmotic pressure of the tissue cells, and how each of these is influenced by a variety of conditions which include blood volume, cardiac activities, the autonomic nervous system, protein concentration and permeability, liver and kidney activities, ions and hormones, osmotic pressure and others.

This interchange of water between the cells of tissues and organs and circulating blood must mean that the body contains means of regulation of the water excretion and the water intake by means of thirst. It has been established that a center in the hypothalamus regulates the entire mechanism of water exchange to muscles, skin, capillaries, and kidneys; and it is believed that the center is affected by glandular influences, especially that of the hypophysis, whose secretion may produce excessive diuresis, as in diabetes insipidus and may be controlled by injection of posterior lobe pituitary extracts. On the other hand injection of posterior pituitary extract may cause a rise of blood pressure with vasodilatation of the kidney vessels and diuresis. This would suggest a hormone with a dual action, one checking undue loss of fluids from the body, and when it is deficient, diuresis may occur.

In diabetes insipidus, serious symptoms develop if water restriction is enforced, due to the uncontrolled loss of tissue water in the urine. Likewise, if the attempt is made to control the excessive secretion of urine by injections of pituitary extract without limita-

tion of the water intake, serious symptoms of water intoxication develop as a result of the excessive water content in the body. These symptoms, consisting of headache, nausea, incoordination, and profound weakness, are similar to symptoms produced in dogs when water is given by the stomach tube in quantities daily approximating the body weight. It is well known that sodium chloride favors the retention of water in the body and in renal insufficiency an excess of salt may lead to the development of edema and in such cases the edema is increased by the ingestion of water.

In suspected edema of the brain, which may occur during an acute hemorrhagic Bright's disease, or idiopathic epilepsy in which it is theoretically assumed that excessive hydration of the central nervous system has occurred, it may be advisable to restrict water intake. In nearly all other conditions, however, one of the most important advances of the past two decades has been the general clinical recognition of the imperative need of adequate body fluid in the treatment of disease. Many patients with prolonged illnesses develop appreciable or marked degree of dehydration in spite of what may appear to be an adequate intake of fluid. Consideration must be given to the constant loss of water occurring through the skin and pulmonary channels. This loss varies from 600 to 800 c. c. and even more when visible sweating occurs. In Bright's disease and other conditions with periodic vomiting and diarrhea, varying degrees of dehydration often develop insidiously. A dry tongue does not always indicate the extent of dehydration, and thirst is an uncertain symptom in many conditions.

In chronic types of Bright's disease, the intake of water may amount to from 3 to 5 times the normal amount of urinary water to carry off the same quantity of urinary solids eliminated in health.

ENDOMETRIOSIS AND ENDOMETRIOMATA*

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There is no subject which has attracted so much attention in gynecology during the past decade as heterotopic or misplaced uterine mucosa. Volumes have been written on the nature of these ectopic endometrial proliferations. Care has been taken to elevate its consideration above the fad level, but the natural enthusiasm following the revelation of a series of theories such as Cullen,[1] Sampson,[2] Novak and Robert Meyer[3] have presented, makes it necessary for us to stop a moment; take stock of the data at hand; appreciate and correlate the facts as they are presented; then map out a scientific well-substantiated conception of this subject which can be utilized not only at the bedside, but also in the operating room. This article is to be a rather brief summary of our present day knowledge and ideas of misplaced endometrial tissues. Maes states that while up to the present time endometriosis has been largely considered the business of the gynecologist, it would seem, in view of the many locations in which it may be found, that surgeons also should become familiar with it. In spite of the great interest shown, there are still many general surgeons and gynecologic surgeons who do not include endometriosis in the differential diagnosis of female pelvic disorders and who fail to recognize the lesions at operation.

By endometriosis is meant the pathologic change brought about when fragments of endometrium leave their proper situation in the uterus and implant themselves in neighboring tissues; and by endometriomata is meant the tumors which develop if conditions are favorable for the growth of these implants. The majority of endometriomata arise in this way, but possibly a small number may be derived from Mullerian rests. An endometrioma is therefore a tumor containing endometrial elements, or at any rate, elements which look and behave like endometrium.

In 1908, Cullen[1] examined and reported his findings on the number of diffuse endometriomata of the uterus and found as a result of his investigation that

"in places there was direct continuity between the endometrium proper and that contained within the tumor, and frequently an actual communication between the uterine cavity and several of the cystic spaces in the growth. This became known as the diverticular series and may be regarded as the simplest form of endometriosis. In certain other uterine endometrioma, no such continuity can be demonstrated, and in these it must be assumed that the misplaced endometrium has reached its new situation by metastasis through the lymph vessels or venous channels of the uterine wall.

"Many theories were advanced to explain the occurrence of extra-uterine endometriomata. Different authorities suggested that they were derived from Wolffian or Mullerian rests or by metaplasia from the peritoneal endothelium. In 1921, however, Sampson[3] eliminated the old problem with his theory of retrograde menstruation and cellular spill. According to this theory, some of the menstrual discharge with its normal content of endometrial fragments may pass backward through the fallopian tubes and so reach the pelvic cavity. The structures lying in closest relationship to the fimbriated end of the tubes naturally receive most of the fragments or implants, as they are now called, but gravity and the normal movements of the bowel and bladder render a much wider dissemination possible.

"The subsequent fate of these implants depends on several factors, among others their vitality and viru-

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lence and the nature and resisting powers of the tissue invaded. The ovary and rectovaginal septum appear to offer the best condition for active proliferation, and it is therefore in these situations that extra-uterine endometriomata are most commonly found. There is always a definite reaction on the part of the invaded structures and this leads to adhesions of great density and to hyperplasia of any fibrous or muscular tissue which may be present in this vicinity. The menstrual products of the tumor itself are also peculiarly irritating and still further intensify the local reaction.

"Endometriosis following direct invasion of the uterine wall from the endometrium usually results in a diffuse tumor, largely made of hyperplastic fibromuscular tissues, but also containing numerous islets of misplaced endometrium, some of which have become cystic and filled with blood. The external contour of the uterus is not usually altered, as the enlargement is uniform. The tumor differs from a fibroid in possessing no capsule and in having its cut surface studded with the endometrial areas already referred to. Like a fibroid, it may occasionally grow outwards or grow inwards and become pedunculated, subserous, interstitial or submucous, as the case may be. In cornual tumors, there is a localized swelling near the inner end of the tube and on section this is frequently found to contain a cyst filled with tarry blood."

Endometriosis following retrograde menstruation and cellular spill produces naked eye appearances which are unmistakable. The fimbriated extremities of the fallopian tubes are usually patent. Dotted about the peritoneal cavity are numerous purplish blebs which microscopic examination will demonstrate to be endometrial implants. Some of these have irritated the peritoneal surface and led to dense adhesions as evidenced by fixation of the ovaries and tucking up of the utero-vesicle or the utero-rectal peritoneum.

"If conditions are favorable for further growth, definite endometriomata are produced. These differ in their naked eye appearance according to the particular organ affected. In the ovary, the physiological activity of the implants, as judged by the amount of blood effused during menstruation, is most marked, and the tumor therefore becomes cystic and filled with tarry blood. The tumor is usually about the size of a walnut, but sometimes much larger and may even reach the dimension of a large unilocular cyst. It is adherent to the original point of implantation and consequently its contents always escape when the ovary is separated at operation. The firm walls of the cyst then prevent complete collapse and the point of rupture remains open and ragged. In addition to the primary adhesions, others are usually present, and these firmly attach the ovary to adjacent structures and when separated expose a raw granular surface. These adhesions probably result from leakage of the irritating cyst contents.

"Next in importance comes the tumor of the rectovaginal space, which develops presumably from an implant in the pouch of Douglas. The appearances are again characteristic, the rectum being tucked up and adherent to the posterior surface of the uterus and its wall much thickened and nodular, sometimes to such a degree that it closely simulates a malignant tumor. The growth may also involve the cervix and posterior vaginal wall, and even project as nodules or polypi into the posterior vaginal fornix.

"The uterine wall itself may develop an endometrioma as a result of endometriosis of the pelvic cavity, implants attaching themselves primarily to the peritoneal surface of the uterus or invading it from a tumor already established in the ovary, rectovaginal space or elsewhere. The direction of the growth is toward the uterine cavity, however, and not away from it as in the diffuse type of tumor."

Similar tumors are not infrequently found on a fallopian tube, round or uterosacral ligaments, pelvic colon, small intestine and more rarely as pathologic curiosities in the appendix, umbilicus, inguinal canal or scar of a previous abdominal operation, or in the labia, perineum or cervix.

The question of other lesions associated with endometrioma is important, and of these, uterine myomas may take first place. These were present in 40 per cent of a number of reported cases, and were of sufficient size to be of clinical importance in 27 per cent. Looking at it from the opposite point of view, 10 per cent of all myomas operated upon are associated with endometriomata.

Endometriosis is possible at any age between puberty and the menopause, but treatment of the resulting endometriomata is usually carried out during the period of sexual maturity. Although such lesions have been found in girls and in elderly women, they are most commonly encountered during the fourth, fifth and sixth decades. It is quite apparent that endometriosis is more common in white women than in colored women, in barren spinsters and women who have had but one pregnancy than in those who have borne many children, and in association with normal tubes rather than with pelvic inflammatory disease. It is not possible to give statistics as to the frequency of endometriosis, but the number of endometriomata producing symptoms is considerable.

During the past five years, the incidence of endometriosis in my private practice has been carefully checked and, much to my surprise, found to be 12.5 per cent of all gynecologic cases operated upon and 28 per cent of all abdominal gynecologic cases. A theory that may clarify the great incidence of this lesion may be offered; in most practices made up of a good class of well-to-do patients, many years of normal menstruation occur before interruption by pregnancy, this being due to late marriage, contra-

ception, and spacing in children, which in turn is due to modern economic factors.

Two types of patients have endometriosis: those who are normal in every way except that marriage, and especially pregnancy, are delayed, and those who have stigma of pelvic underdevelopment. The latter often do not marry and, if they do, frequently do not conceive. It would seem, if this is true, that it would be better that there be earlier marriages and that contraception be put off until at least one or two pregnancies have occurred.

In its earliest stages, endometriosis produces few symptoms for which it can be held responsible and may be discovered only accidentally when the abdomen is opened for some other condition. The implants mature and adhesions form, however, and there will be increased pelvic discomfort, dysmenorrhea and disturbances of the menstrual flow. Even then, certain associated lesions, such as fibroids or malignant diseases, may dominate the clinical picture and produce the symptoms for which the patient actually seeks advice.

Regarding symptoms, there is not one which will definitely point to the existence of endometrioma. Lower abdominal pain is very common and in our series was present in 40 per cent of the cases. Dysmenorrhea, particularly of recent origin, is probably the most characteristic symptom, but it is by no means constant, and was complained of in only 30 per cent of our cases. Menorrhagia, or epimenorrhagia, is another common symptom and was also found in approximately 30 per cent of our cases. Bearing down and rectal discomfort are frequently met with when the growths are in the rectovaginal space, or when there are adhesions in the neighborhood of the rectal wall. Backache is such a common complaint in women that its value in differential diagnosis is strictly limited, but this symptom is prominent when the ovaries are adherent in the *cul-de-sac,* or when the rectum or posterior wall of the cervix is involved. Dyspareunia is frequently complained of in similar circumstances; also shooting or electric pains extending down into the uterus and the vagina. Occasionally there may be pain down one or other legs when an ovarian endometrioma is adherent to the pelvic wall. Marked constipation may be associated with extensive involvement of the rectum or other parts of the alimentary tract, and a blood stained discharge may be present if the rectovaginal growth has perforated the vaginal wall.

The physical signs naturally depend upon the situation of the tumor. In the ordinary diffuse uterine tumor there will usually be moderate and uniform enlargement of the uterus, but with cornual tumors there may be definite irregularities. In either case, the physical signs will closely resemble those of uterine myoma and differential diagnosis will be impossible unless increasingly severe dysmenorrhea has led one to suspect the true state of affairs.

In ovarian endometrioma, there will be an enlargement and fixation of one or both ovaries, and as these are usually adherent to the back of the uterus, the latter will be retroposed and its mobility lessened. In the absence of evidence pointing to pelvic infection, such findings should lead one to suspect an endometrial tumor.

When the growth is in the rectovaginal space, physical signs are most characteristic; the infiltrating character of the tumor and the presence of tender, shotty nodules in the wall of the posterior fornix are sufficient evidence upon which to base a diagnosis. Rectovaginal examination will prove helpful in these cases, as it may reveal fixation of the rectum to the back of the tumor.

That endometriomata seriously interfere with child-bearing is shown by the fact that patients with these tumors usually give a history of sterility or of no birth's having occurred for several years. In our series, this has been the case. However, endometrioma in its early stages is not an absolute bar to pregnancy.

As endometriomata are usually widely distributed and of an infiltrating character, it will be understood that conservative measures are possible only in the early stages, and that even then the chances of return are considerable. A conservative policy is justifiable, however, only if one ovary alone is involved, or if there are isolated nodules in the rectovaginal space causing dyspareunia.

Operation is the procedure of choice. Treatment of cases in which there is slight involvement of the ovaries, and in which adhesions are not extensive, merits careful consideration. Numerous factors must be considered: the age of the patient, her social status and desire for children, as well as the extent of the lesions. The surgeon is never justified in removing both tubes, ovaries and the uterus just because small endometrial growths are present. Frequently the lesions themselves can be removed, a normal uterus with tube or tubes, ovary or part of both

ovaries can be left behind and the patient restored to good health. The patient may bear children and be saved from the harrowing miseries of a premature menopause, although it may be necessary at a later date to do a complete operation. The majority of patients willingly undergo a second laparotomy if they can be given a chance of conceiving and be spared menopausal symptoms for a few years. Not all cases have to be reoperated upon, for in some the disease never advances again to a point where the patient has symptoms. Unfortunately, many women present themselves when the disease is so far advanced and widespread that conservatism would be foolish. In such cases, radical operation is not only indicated, but necessary and unavoidable.

Local growths in the umbilicus, abdominal scars, groin, vulva, vagina and cervix should be removed carefully. To leave behind any of the Mullerian tissue may mean a recurrence of the lesion.

In diffuse adenomyoma of the uterus, supravaginal hysterectomy is adequate for a cure. However, be assured that there are no cervical growths.

When there is involvement of the rectovaginal septum, the rectum is almost invariably invaded and the ovaries are badly diseased as well. Panhysterectomy should be performed. Often it is better to amputate the vaginal cuff before dissecting the adenomyoma free from the rectum. If the bowel involvement is deep-seated, it is wiser to sacrifice tumor than rectum, since double oophorectomy is usually indicated. Any tissue left in the pelvis of an endometrial nature will regress and the patient will experience no further discomfort from it. However, the attendant fibrosis and adhesions may cause the patient some inconvenience.

Radium as a method of treating misplaced endometrium is not yet catalogued with certainty. Theoretically, it is ideal if the patient is near the menopause. Ovarian function is thus destroyed, and local lesions in consequence regress, but there would be no improvement in the accompanying fibrous tissue and smooth muscle formation. If there is a chance for conservative surgery, it is much to be preferred; especially is operation indicated when any suspicion of carcinoma, tuberculosis or salpingitis is entertained.

It is well to bear in mind when treating misplaced endometrium that one is dealing with tissue which is under the control of ovarian stimulation. In other words, ablation of the ovaries means spontaneous recession of endometrial growth; and partial removal of the growth with ovarian tissue intact does not insure a permanent cure for the patient. However, making an operative diagnosis of pelvic endometriosis is not a prima facie indication for removal of both ovaries. If nothing else, this resumé is meant to sound a healthy note of conservatism.

No doubt the majority of cases of pelvic endometriosis found recently are mild and are of only academic interest. Not infrequently the lesions are chance operative findings and are too minute to cause symptoms, although they might well progress later to a stage where the patient's comfort and health would be seriously affected.

The prognosis after operative interference is excellent. Late results are most gratifying. We have observed an interesting postoperative complication to which a case of pelvic endometriosis seemed to be susceptible. It is occasionally true when there is a bowel involvement that these patients suffer from obstinate distention and even from partial intestinal obstruction. The same alarming symptoms at times have been observed during the first menstrual period following laparotomy. In both instances, expectant treatment gives excellent results.

Without operation, advanced cases lead a wretched life. They suffer excruciating pain at each menstrual period and soon become bedridden, and extensive involvement of the bowel may lead to partial and later complete intestinal obstruction.

There is another indication for surgical interference. As pointed out by Sampson,[2] misplaced endometrial tissue can undergo malignant change just as adenocarcinoma can develop in the uterine cavity. Such an etiology may well explain many peculiar pelvic carcinomata which thus far have defeated all attempts at classification.

CONCLUSION

Adenomyomata of the uterus, endometrial cysts of the ovaries and pelvic endometriosis are among the most interesting conditions with which gynecologists have to deal. They are diagnosed microscopically by the presence of uterine glands and stroma in misplaced locations. How they arise in these sites is a disputed point. Invasions best explain adenomyoma of the uterus. Transplantation is the most probable cause of

adenomyomata in postoperative abdominal scars. Developmentally misplaced Mullerian tissue offers the most plausible explanation for the endometrium in the umbilicus, groin and vulva. Either metaplasia of the pelvic peritoneum or developmentally Mullerian tissue could easily account for the variety of lesions found in pelvic endometriosis and endometrial cysts of the ovaries. The treatment is operation: conservative operation when possible, radical operation when necessary. Removal of the ovaries means spontaneous regression of the individual lesion, as it means a senile change in the mucosal lining of the uterus.

An attempt has been made to review a subject in which unusual interest has been manifested, and about which new facts are daily being presented. If the next decade adds as much to our knowledge of misplaced endometrium as has the past twenty years, it will not be long before some of the disputed points as to the origin of heterotopic endometrium will be settled. Then facts will displace present day theories.

BIBLIOGRAPHY

1. Cullen, T. S.: N. Y. State Med. Jour., **19**:295, 1919.
Arch. Surg., **1**:215, 1920.
Bull. Johns Hopk. Hosp., **7**:112, 1896; **9**:142, 1898.
Surg., Gyn. & Obst., **22**:258, 1916.
Trans. Sou. Surg. & Gyn. Assn., **24**:475, 1912.
The Umbilicus and Its Diseases. Philadelphia: W. B. Saunders Co., 1916.
J.A.M.A., **62**:835, 1914; **67**:401, 1916.
Adenomyoma of the Uterus. Philadelphia: W. B. Saunders Co., 1908.
2. Sampson, J. A.: Amer. Jour. Obst., **78**:161, 1918.
Arch. Surg., **3**:245, 1921.
Amer. Jour. Obst. & Gyn., **10**:649, 1925; **14**:422, 1927.
Amer. Jour. Path., **3**:93, 1927.
Amer. Jour. Obst. & Gyn., **12**:459, 1926.
3. Meyer, Robert: In Veits Handbuch der Gynakologie Weisbaden, **1**:413. J. F. Bergman, 1907.
Zentralbe F Gynakologie, **49**:2121, 1925.
Ztsche F Geburtsh u Gynakologie, **43**:130, 1900.

DISCUSSION (*Abstract*)

Dr. M. Y. Dabney, Birmingham, Ala.—Dr. Bertner's summary of the subject of endometrioma would make any comments seem feeble repetitions. But the condition is found so frequently in abdominal sections, and is diagnosed preoperatively so infrequently, that it is a timely subject in any gathering of gynecologists.

The great problems are: the earlier diagnosis of the disease and exactly what is best for the patient. Unfortunately, the patients are often women who are desirous of offspring; and the treatment as well as the disease may lessen fertility.

Complete excision of the involved tissues, wherever possible, will check the progress of the condition, but that is often more easily said than done. Deep x-ray treatment or irradiation with radium to destroy ovarian function will accomplish the desired result, but will bring on an artificial menopause.

Most surgeons now-a-days have swung to the conservative side and only excise diseased tissue, ovarian or otherwise, wherever possible, both to favor future conceptions and to prolong the menstrual life of the individual, feeling that if there is a troublesome recurrence, recourse can always be had later to irradiation.

Many years may be passed by the patient without discomfort; but one must always bear in mind the fact that the dense adhesions and inflammatory tissue of endometriosis will persist even after irradiation castration. In fact, no pelvic adhesions are denser, except perhaps those from streptococcic infection.

Surgery in some cases will have to precede or succeed irradiation. For example, intestinal obstruction, partial or complete, is a complication which irradiation cannot relieve. This has been encountered in my own practice, although fecal fistula, mentioned by Dr. Bertner, I have been blessed by not encountering. Implantation upon the vaginal cervix has been the rarest type of complication observed by me.

Where a large cystic mass is present and is accompanied by elevation of temperature one cannot rule out infected ovarian cyst, in which case irradiation would only make matters worse. Similarly, even a partial intestinal obstruction, as revealed by the history and roentgenologic study, would make surgery definitely preferable.

I agree with Dr. Bertner that surgery in the main is more conservative in the childbearing period, because often it can relieve pain through the removal of diseased tissue, and above all, because it affords a definite diagnosis and determines whether a malignant change has taken place. In the latter instance, a sterilizing dosage of radium or x-ray, which might have been employed had no section been performed, can be increased in amount to combat the malignancy.

No disease of the pelvis tests the judgment of the gynecologic surgeon more than does endometriosis.

Dr. Quitman U. Newell, St. Louis, Mo.—Endometriosis is one of the major gynecologic problems of today. It has been found in almost every part of the abdominal and pelvic cavities. Pelvic endometriosis has a definite line of symptoms, most of which are very difficult to handle. Every time the patient menstruates the pelvic organs undergo marked changes; and relief of these changes can be accomplished by stopping menstruation. In order to stop menstruation it is necessary to castrate the patient either by surgery or irradiation; and this is not always the best for the patient. No young girl wishes to be castrated unless it is absolutely the last resort, so we often try many remedies to relieve these symptoms, without avail.

Dr. John Zell Gaston, Houston, Tex.—I should like to ask the speaker whether he has noticed a difference in the frequency of endometriosis in his charity and private patients.

Dr. Karl John Karnaky, Houston, Tex.—The endometrial implants (endometriosis) undergo the same changes as the normal uterine mucosa. So one can see why Dr. Bertner's patients complained of pain in the pelvis, because blood comes from these implants as from uterine mucosa, and flows over the peritoneum. Also the implants grow into the surrounding organs and cause firm adhesions to adjacent structures. They should not be separated if they are adherent to the intestines.

A clue to a diagnosis of endometriosis when the abdo-

men is opened is this: if tubal adhesions are easily freed, then one suspects gonorrhea or some other infection as the origin; if they are dense, one suspects endometriosis. I agree with Dr. Bertner about the fixation of the female pelvic organs in many cases of endometriosis. This has been confirmed many times in the gynecologic operative clinic at the Jefferson Davis Hospital. Also a fullness of the *cul-de-sac* is a suggestive finding; but other conditions have to be ruled out.

Endometriosis is common, and one should be on the lookout for purplish spots in every vaginal examination and in the abdomen of every woman operated upon. Endometriosis occurs in 25 per cent of all fibroids and in 10 per cent of all women operated upon abdominally.

Occurrences are most common in and on the ovary and in the pouch of Douglas.

Where extensive endometriosis is encountered in a patient who has four to six children, one is more justified in removing merely the ovaries, which will lead to an absorption of the adhesions.

I have performed nine ovarian neurotomies and presacral sympathectomies in nine cases of endometriosis. All of them have obtained relief from their pain. We suggest leaving the ovaries in and doing ovarian neurotomy and presacral sympathectomy when the endometriosis is only on ovaries, tubes and uterus. Dr. Counseller and Dr. Willard R. Cooke advocate these operations in endometriosis. In our nine cases relief was obtained from pain and yet the patients had ovarian function with normal menstruation. It is better to leave the ovaries in even if they seem almost destroyed, and to resect the nerves if the patient is a young woman.

I do not agree that these women have menorrhagia and epimenorrhagia as one of their complaints. This is not logical because the endometrium is not affected, and in most cases there is plenty of normal ovarian tissue left even if the endometriosis involves one or both ovaries. We have not found menstrual disorders any more common in endometriosis than in non-endometritic cases. If the ovaries are destroyed by the endometriosis then we should see hypomenorrhea or amenorrhea. We have about 200 cases of endometriosis now in our clinic, so we previously apparently overlooked this condition.

We had two cases of death due to endometriosis because we tried to free the adhesions from the rectum, thinking they were just simple inflammatory adhesions. These two women died from perforated gut. I believe that endometriosis is a great factor in our mortality in gynecologic operations. The adhesion may have been just a small one to the gut deep in the pelvis and we pulled it loose, making a small hole in the gut with subsequent peritonitis and death. We suggest that a piece of uterus be removed whenever freeing adhesions of gut to uterus instead of looking for the line of cleavage. Radium is not used because if the rectum is bound to the posterior aspect of the uterus, one may get rectovaginal or uterine fistula. One of the worst cases of endometriosis that I have ever seen was in a case of stenosis of the cervix from endocervical cauterization. I have never seen a case of endometriosis from conization of a cervix with stenosis. Cervical stenosis is one of the causes of endometriosis in our series.

Endometriosis has been produced experimentally in the uterine wall by sticking a large needle through the uterine wall and into the endometrium. While withdrawing the needle slowly, suction was made and the results were endometrial implants in the uterine wall producing endometriosis.

Dr. Bertner (*closing*).—In answer to Dr. Gaston's question, I will say the incidence of endometriosis is far greater in private than in charity practice, which is probably explained by the fact that charity practice is largely colored women in which endometriosis is rare.

WIDESPREAD MISUSE OF ENDOCRINE PRODUCTS IN THE TREATMENT OF GYNECOLOGICAL SYMPTOMS*

By GRIDER PENICK, M.D., F.A.C.S.
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The enormous increase in the use of commercial preparations of hormonal nature, especially those related to the female sex, has been a very striking thing. One may well wonder whether this will prove to be a permanent thing or whether it will gradually decrease and go the way of some medical fads of the past. This will depend on only one thing, namely, whether or not good is accomplished by their use.

To state the above points in another way, it might be said that the problem I have been asked to discuss is a very complex one. A final answer cannot be given now due to our lack of knowledge. It would seem that the simplest way to handle this question would be to say that we had better determine the rational uses of these preparations and consider all other uses as "misuses." It is granted that there are many controversial opinions about their uses and dangers. These controversial points will require much more study before they can be settled. It is evident that much of the literature that has come out in regard to female sex hormonology has been written by men who had become a little bit overenthusiastic about their subject. In fact, one of the most striking things in the literature is an almost total lack of reports of failures in cases where these endocrine preparations have been used in treatment. Many of these reports cover such a small series that they are almost worthless in so far as proving anything.

Another point in regard to the literature: I

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venture to state that the average practicing physician is much more conversant with the statements made to him by some more or less high-powered drug salesmen than he is with the reports furnished by the Council on Pharmacy and Chemistry of the American Medical Association.

I doubt very much whether it is safe to allow a new preparation to be used indiscriminately before it has been worked out thoroughly by a group of experts in that line, so that the indications, contraindications and dosage are known and understood. If a new discovery has sufficient merit it will soon find its way into the standard textbooks. All of us are familiar with the numerous so-called preliminary reports in our journals which extol the virtues of some new form of treatment, which frequently is never heard of again. Sometimes physicians are led to try out new, unproven and even dangerous forms of treatment by too much premature publicity; for example, remember the recent tragedies connected with elixir of sulfanilamide.

I shall discuss only the two ovarian hormones, estrogen and progestin, and the anterior pituitary and anterior pituitary-like substances. The thyroid and other closely related glands will, of necessity, have to be left out.

Let us begin by outlining briefly the glandular forces concerned in a normal menstrual cycle. It is the consensus of opinion among the better gynecologists of the country that some such mechanism as the following is what occurs: Under stimulation of a substance formed in the anterior pituitary (called prolan A) a follicle enlarges till it ripens and bursts. This occupies approximately the first 14 days of the cycle, starting the count immediately after the cessation of the flow. By this process the concentration of the follicular hormone in the blood stream is constantly being increased these 14 days. When this concentration becomes sufficient, two things happen. First, ovulation occurs. Second, the marked increase of the blood concentration of estrogenic hormone automatically cuts off the supply of prolan A and stimulates the anterior pituitary to form another substance, called prolan B. Now prolan B stimulates the formation of corpus luteum just as prolan A stimulates formation of the estrogenic hormone. So we see that the ovary is stimulated to form two different hormones because of stimulation by two different substances elaborated in the anterior pituitary. It is well to note here that each of the two ovarian hormones has a depressing effect on the anterior pituitary, exerted in such a way that when the concentration of estrogen in the blood stream reaches a certain point, the supply of prolan A is turned off and prolan B turned on. Then when the corpus luteum concentration reaches a certain point the prolan B is turned off and prolan A turned on, which initiates another cycle. We must therefore consider that the endocrine influences which affect and cause menstruation are multiple, closely interlocked and delicately balanced. It follows, then, that this balance may be upset if any one or more of the four above named substances is absent or is present in an abnormal quantity, either increased or decreased. The above statement applies not only to menstruation, but to many of the so-called secondary sex characteristics.

In the above paragraph the terms prolan A and B were used when, strictly speaking, pituitary I and II should have been used. This was done because I felt there was less likelihood of confusing my hearers. I realize that the terms prolan A and B should be restricted to descriptions of the chorionic gonadotropic hormone found in pregnancy urine.

With the foregoing remarks in mind, let us examine some of these substances and try to evaluate properly their worth. For purposes of clarity I shall divide the discussion of each group into the following six subjects:

(I) Nomenclature.

(II) Standardization (and assay).

(III) Indications.

(IV) Contraindications, including not only immediate and remote effects which may produce more harm than good, but also some conditions formerly thought amenable to treatment by the agent, but now proven not to be.

(V) *Dosage.*—If the dosage has not been worked out or if one is not thoroughly familiar with it, the preparation should not be used. It is axiomatic that the smallest dosage that will produce results is the one which should be used.

(VI) Methods of administration.

EXTRACTS OF ANTERIOR PITUITARY SUBSTANCE

Nomenclature.—The Council on Pharmacy and Chemistry of the American Medical Association says: "Owing to the present unsettled state of investigations into the nature of the pituitary and related principles, the Advisory

Committee considered it inexpedient to attempt to formulate a definite nomenclature for this group of substances."

Standardization, Indications, Contraindications, and Method of Administration.—To save time, the above topics may all be handled together. There are only two preparations on the American market at this time which have attained much prominence: "gynatrin" (Searle) and "prephysin" (Chappel). The indications have not been worked out yet. The most important contraindications to their use are that while these preparations unquestionably contain gonadotropic factors, they also contain others which act on the thyroid, breast, pancreas, and so on. Our knowledge has not advanced far enough to allow us to know what far-reaching effects may be obtained by their use. The dosage is not well worked out. These extracts are to be given hypodermatically. It has been definitely shown that desiccated anterior pituitary for oral administration is valueless.

Anterior Pituitary-Like Preparations.—The urine of pregnant women, castrates and postmenopausal women contains gonadotropic principles which in some ways are like the principles obtained from the anterior pituitary. The urine of pregnant women is rich in prolan B, while the urine of castrates and postmenopausal women contains a larger percentage of the follicle stimulating substance, prolan A. It seems to be well established that the origin of the gonadotropic principles in pregnancy urine is the placenta, not the anterior pituitary, as was formerly supposed. These are the substances upon which the pregnancy tests of Aschheim-Zondek and Friedmann depend.

Numerous American pharmaceutical houses manufacture these preparations. Some of these with which you are probably familiar are "antuitrin S" (Parke, Davis & Company), "antophysin" (Winthrop), "follutein" (Squibb), and "A. P. L." (Ayerst, McKenna & Harrison). Some of these are derived from placenta, others from pregnancy urine.

Nomenclature.—What I wrote in regard to the anterior pituitary extracts applies here also.

Standardization and Assay.—In all of these preparations the rat is used as the test animal. However, all four of them differ as to the technic of the test and as to criteria. All of these preparations are unstable and deteriorate rather rapidly.

Indications.—Unquestionably some clinical men, as well as some manufacturers, have in the past claimed too much for these preparations. The present consensus of opinion among the better informed clinical gynecologists is that their main function in our armamentarium is their ability to check certain cases of "functional bleeding."[1,2] It is not known just how this occurs, since a case has never yet been found in which human ovaries were luteinized as a result of treatment with anterior pituitary-like hormone. Rodents' ovaries can be luteinized by their use; nevertheless, these drugs do have a place because of this therapeutic result.

Contraindications.—First, before treating a woman for "functional bleeding," extremely careful examinations (even including curettement, with examination of the scrapings by a competent pathologist) must be done. This is done to rule out carcinoma or submucous fibroids. It has been pretty well demonstrated by now that the anterior pituitary-like preparations will not accomplish much in such conditions as amenorrhea, primary dysmenorrhea, habitual abortion, acne, migraine and Fröhlich's syndrome, conditions for which they were advised a short while back.

Dosage.—In cases of functional bleeding, 100 to 200 rat units daily for a period of a week may be used. If this amount, when combined with other forms of treatment used in hemorrhage cases, does not produce marked change for the better, other treatment had better be instituted.

Method of Administration.—Dried extracts of anterior pituitary are inert when given orally. These preparations are to be given intramuscularly. Sufficient work has not been done on the gonadotropic principles obtainable from pregnant mare's serum or urine to make any positive statements in a paper of this kind, but apparently those two sources will, in the future, supply potent preparations.

ESTROGENIC HORMONE

Nomenclature.—The enormous amount of bewildering literature on these substances that has flooded medical and kindred literature recently has been confusing, partially because of the fact that many authors have coined their own terminology. This is true in other languages as well as our own. In an attempt to simplify this situation the Advisory Committee of the Council recommends the following terminology be used: estrogenic, an adjective to de-

scribe any substance that produces estrus. Estrogen, a noun, to be used as a collective term for all substances having this property. They further recommend that the terms theelin, theelol and dihydrotheelin be used respectively in place of estrone, estriol and estradiol. Some of these terms were formerly registered trade-marks, but the companies owning them have agreed to relinquish any proprietary rights they had in the names.

Standardization.—Several methods of assay are used, most depending on cornifications of the vagina of a rodent. In general, biological assays are uncertain, one unbiased observer stating that an error of 1,000 per cent frequently occurs. Other factors that create uncertainty when estimating the potency of samples of estrogenic substances are: (1) the inherent variability of test animals, (2) the lack of uniformity in the technic of conducting the assays, and (3) the most important, the differences in sensitivity of various species. In other words, we have no proof that just because a certain effect is produced in a rat, the same effect will be produced in a woman. There is no proof that just because two preparations are equally effective in cornifying the vaginal mucous membrane of a rat that they will prove equally effective in relieving castration phenomena in a woman. From a clinical point of view, cornification of the vaginal mucous membrane is of importance only in the treatment of juvenile gonorrhea.

In regard to units of measure there are three: the mouse, the rat and the international. The last named is the only absolute unit. It represents the amount of estrogenic activity in one-tenth microgram of crystallized theelin. Roughly, one mouse unit is approximately one-fifth rat unit. The ratio of the international unit to the rat unit varies from 1:3.3 to 1:8, depending on the unit of the company which is being used for comparison. We see from this, then, that we really know very little about the contents of a commercial ampoule, regardless of the dosage marked on it.

Accurate quantitative assay of the blood and urine estrogen concentration in women is very difficult. Only a few laboratories are equipped for this. It is to be noted that there is much variation in supposed normal amounts when results from different laboratories are checked against each other. I believe the figures obtained by Frank[3] are considered to be as reliable as any we have. Multiple determinations on 150 women showed that the concentration curves of the blood and urine are approximately parallel. The curve in the blood gradually ascends till ovulation, when a small peak is formed. Following this, it descends slightly, but comes back and reaches a second, higher peak, which abruptly drops just before the onset of the flow.

The blood and urine concentration at the height of the peak is usually about 25 mouse units per liter. Frank has found that the average normal woman manufactures and eliminates about 1,500 mouse units per month. Our hypothesis, then, must be that if a normal woman of menstrual age forms less than 1,500 mouse units per month, she needs more. If she forms more than 1,500, she has too much. We may agree, therefore, that a woman should be given estrogenic hormone only if she has too little, and then the amount of utilizable hormone given her must be only the difference between the amount she has and 1,500 mouse units, not more than this.

Indications.—Since our only real indication for the use of estrogenic substance is a proven hypoestrinism and since most men have not laboratory facilities to determine this, most estrogen that is given is used empirically. Of all the flattering claims that have been made for estrogen, only a few can be proven when subjected to rigidly controlled scientific tests. Psychic factors make an evaluation of the worth of these preparations extremely difficult. The majority of men who are competent in this line recognize only three positive indications for estrogenic therapy. They are (1) certain cases of vasomotor menopausal symptoms, (2) senile vulvovaginal changes, and (3) juvenile gonorrheal vaginitis.

Dosage.—In certain cases where vasomotor symptoms are especially troublesome when associated with the menopause, estrogenic therapy may be used. It is certainly *not* indicated in all women at the time of the menopause, simply because most of them do not need it. At times of emotional stress, however, these symptoms are liable to become exaggerated and it is well to tide these women over these times with estrogen. The suggested dosage is 2,500 to 3,000 international units to be given over a period of two to four weeks. If a crystalline preparation or solution is given orally, four or five times this dosage must be used to get the proper amount of utilizable hormone. It is to be borne in mind that estrogenic hormone is all eliminated within 96 hours after administration (sometimes much

more rapidly), so it is well to give small doses oftener rather than larger doses less frequently.

In the other two conditions named treatment is more efficacious when vaginal suppositories are used. In senile vaginitis a 50 or 75 international unit suppository may be inserted each evening for 2 or 3 weeks. If improvement occurs it will be evident in this length of time. In juvenile gonorrheal vaginitis 50 international units may be used till a total of 2,100 units have been given. This is usually all that is necessary.

These figures are more or less empirical, but are based on averages of the estimates of several clinicians. It is unfortunate that as yet we have no accurate laboratory methods to control estrogen therapy such as we have for controlling treatment with thyroid or insulin.

There are numerous good commercial estrogens on the market at this time. Most of them are derived from pregnancy urine (women and mares), placenta or amniotic fluid. They may be obtained in forms to be administered orally, intramuscularly or by vaginal suppository. Some of the better known oral preparations are "progynon" tablets, theelol "kapseals," "amniotin" capsules and emmenin solution. These preparations are not to be confused with desiccated ovarian residue, which is probably inert. Some of the better known estrogenic preparations for hypodermic use are theelin, "amniotin," "progynon" (and "progynon B"), and "sistomensin." These preparations are available in various sized dosage ampoules, from 5 rat units up to many thousand international units per c. c. Examples of estrogenic vaginal suppositories are the theelin and "amniotin" suppositories.

Contraindications.—It must be borne in mind that estrogen therapy is only replacement therapy. Claims made that it "stimulates the ovary" are certainly unfounded. In fact, the opposite is true. We must remember that when the blood estrogen level becomes sufficiently high this depresses the cells of the anterior pituitary which form the substance which stimulates the ovary to form estrogen; so that in reality the use of excessive amounts of estrogenic therapy actually decreases the amount of estrogen formed in the patient's ovaries.

In addition to this depression of the anterior pituitary mechanism by excessive amounts of estrogen, we have other dangers. Our modern conception of the etiology of three related conditions, namely, hypertrophied endometrium, uterine polypi and uterine fibromyomata, is based on the premise of hyperestrinism.

Before giving long-continued or large doses of estrogenic therapy, we must consider the possibility of producing malignant changes in the breast. At the present time, in spite of an enormous amount of experimental work along this line, it is impossible to make positive statements about this. We do know, however, that clinically carcinoma of the breast seems to grow much less virulently after total ablation of ovarian function. It is therefore believed that estrogen should be given with extreme caution to women who have breast disease or family history of cancer.

Claims have been made in the past of advantages of estrogenic therapy in numerous conditions in which it is now believed not to be beneficial. Among these conditions are amenorrhea, primary dysmenorrhea, hyperemesis gravidarum, acne, frigidity, hypertension, sterility, hemophilia, painful breasts, premenstrual tension, involution psychosis and arthritis. In many of these conditions, estrogenic therapy not only does no good, but is contraindicated because some of them are associated with a hyperestrinism.

LUTEINIZING HORMONE

Nomenclature.—Since the discovery of this hormone and the proof of its existence, the work done on it in various countries has been reported in great profusion. This hormone has been extracted from the ovaries of animals and has been manufactured synthetically. Chemically it has a structural formula very much like theelin. In an attempt to simplify the terminology of this substance the Advisory Committee of the Council on Pharmacy and Chemistry of the American Medical Association recommends that "progesterone be the name applied to indicate the chemically pure substance that is the luteinizing hormone and that progestin be used as a general term to describe the substance progestin without reference to the state of chemical purity for convenience in clinical and biological speech and writing." In this paper the term progestin will be used to indicate the luteinizing factor.

Standardization.—The international unit is the amount of progestational activity present in 1 milligram of progesterone. The adult female rabbit is the test animal used.

Indications.—Since the function of this hormone is one of preparing the endometrium to

receive and nourish the impregnated ovum, it would follow that a lack of the proper amount of it might be a causative factor in some cases of sterility and habitual abortion. Unfortunately progestin has not so far been shown to be of value in sterility. It has been shown to be of value in habitual abortion.

In certain cases of uterine bleeding associated with an over supply of estrogen, progestin is of value because of its antagonistic effect to estrogen.

In cases of pelvic operations during pregnancy, progestin has a beneficial effect.

Contraindications.—A fairly comprehensive search of the literature fails to reveal mention or proof of dangers associated with overdosage of progestin comparable to those associated with overdosage of estrogen.

In addition to sterility, there are other conditions for which progestin has been advised, but in which, also, it has proven to be of no value. Among these is dysmenorrhea. Theoretically useful because of its sedating action on uterine musculature, it has been clinically proven of no value in this condition.

It has been advised in cases of amenorrhea; clinically, it is useless here. It is difficult to understand why one would advise its use here. The luteinizing hormone has nothing to do with preparation of the endometrium in so far as the menstrual bleeding is concerned. In fact, menstrual bleeding can be inhibited in some of the lower animals by using progestin.

Dosage.—In cases of habitual abortion it is suggested that one or two international units be given daily for a week each month, the week to be the time that the patient would have menstruated had not pregnancy intervened. This may be continued till the fetus is viable.

In cases of uterine bleeding associated with hyperestrinism, one or two international units daily for one week is advised, in addition to other usual management of this condition.

In cases of pelvic operation during pregnancy, one or two international units daily for 10 to 14 days is given. In this condition, as many as 5 units have been given daily for the first few days with no bad after-effects noticeable.

Method of Administration.—Any of the standard commercial preparations, of which "proluton" (Schering), "progestin organon" and "lipolutin" (improved, Parke, Davis & Company) are examples, may be used. These are oily preparations to be injected intramuscularly. It has been shown that desiccated corpus luteum has no luteinizing effect when given orally.

REMARKS ON FEMALE SEX HORMONE THERAPY IN GENERAL: SUMMARY

One needs only to go into the literature to see how much confusion exists among the writers. A few years ago claims were being made for preparations which we now know are inert. Discovery of the role played by the anterior pituitary and the delicate balance between its hormones and those of the ovary changed the entire conception of the phenomenon of menstruation. An enormous amount of work has been done and is being continued now. Progress has been made in laboratory determinations of blood and urine content of various hormones. Progress has been made in obtaining potent preparations for experiment and therapy. The hormone business may be classed as being big business. The amount expended by the public each year for these preparations undoubtedly runs up into very large figures. It is the duty of the physician to see that they get value received for their money. Many manufacturers are cooperating wholeheartedly. Some of them are spending money on research and are really trying to work these questionable points out scientifically. Some companies, however, are still manufacturing, advertising and selling preparations that should not be on the market. For example: there are still on the market numerous "shotgun" polyglandular mixtures for oral administration. Some of them are in liquid form, others in tablet form. After aging, the proportion of active principle present (if any) changes from what it was when the tablet was new. No one knows what happens chemically when liquid extracts of various endocrine preparations are mixed. It is not necessary to use these empirical mixtures. If two or more extracts are definitely indicated, they may be given separately.

We need literature that is more complete; reporting a few successful cases under conditions which are not controlled is of no value in evaluating the worth of any therapeutic preparation. This is doubly true when reports of the failures are left out of the record.

By and large, one may say with sureness that female sex hormone therapy has been exceedingly disappointing. Back in the days when we advised women to carry around thyroid extract in one hand and desiccated corpus luteum in the other, with instructions to take a bite of each

occasionally, we thought the millennium had come. Since that time there have been developed active principles of estrogenic, gonadotropic and luteinizing hormones, but we still have at least as large a percentage of our women with functional female sex disorders as formerly, if not a greater percentage.

I do not wish to be understood as belittling female sex hormone therapy. I think there are cases where such treatment is indicated. I do believe, however, that there are many women being treated with these preparations now who would be better off on other forms of treatment. Some of these patients present baffling symptoms. Sometimes the doctor does not know just what to do, so he gives them some new hormonal preparation. I do not believe we are justified in practicing that way. If we must do it, let us at least use very small doses.

It might be that this recent female sex hormone therapy craze is dying down somewhat. I believe some of the formerly staunch advocates of it are now shifting to vitamin therapy. The recent vogue of combining numerous alphabetical vitamins is reminiscent of the apparent race between some of the manufacturers of sex hormone products a while back, each trying to market a preparation with more units per c. c. than the other.

Let us try to remain level-headed on this question. Let us use these preparations only when we have a definite indication for them. Let us apply the adage of the old medical preceptor who said: "Gentlemen, we have little business injecting drugs, of which we know little, into bodies, of which we know less."

REFERENCES

1. Novak, E.: A Summarizing Appraisal of Gynecological Endocrinology and Organotherapy. Mellon Lecture, Universitty of Pittsburgh, 1933.
2. Novak, E.: Therapeutic Use of Estrogenic Substances, Glandular, Phys. and Therapy, pp. 193, 211. Chicago: Amer. Med. Assn. Press, 1936.
3. Frank, R. T.: Sex Endocrine Factors in Blood and Urine. Glandular Phys. and Therapy, pp. 219, 229. Chicago: Amer. Med. Assn. Press, 1936.
4. Allen, E.: Menstruation: Glandular Physiology and Therapy. J.A.M.A., press 1936, pp. 163-177.
5. Garner, G. W.: Corpus Luteum Therapy: Glandular Physiology and Therapy. Amer. Med. Assn. press, 1936, pp. 211, 219.
6. Geist, S.: Reaction of Mature Human Ovary to Antuitrin S. Amer. Jour. Obst. & Gyn., **26**:588-592 (Oct.) 1933.
7. Geschickter, C. F.; and Lewis, Dean: Tumors of the Breast Related to Estrogenic Hormone. Amer. Jour. Cancer, **21**: 828 (Aug.) 1934.
8. Mazer, C.; and Goldstein, L.: Clinical Endocrinology of the Female. Philadelphia: W. B. Saunders & Co., 1932.

THE TREATMENT OF INFANT VULVOVAGINITIS WITH ESTROGENIC HORMONE*

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The treatment of vulvovaginitis of infants and children has undergone considerable modification and improvement in the past decade. The treatment in vogue ten years ago involved cleansing the vagina thoroughly, and instillation of various germicidal agents such as potassium permanganate solution, ammoniated mercury paste, mercurochrome, silver nitrate jelly, and a host of other similar remedies. But the results obtained with this type of therapy were, in general, very unsatisfactory, with long periods of treatment, high incidences of recurrence, and low percentages of cure. The time required to accomplish a carefully considered "cure" of the condition involved months of treatment. As a result of the inability to control satisfactorily the disease, biologic means were attempted. Nonspecific protein therapy, immune horse serum, gonotoxin filtrates and vaccines were employed with little or no more success. When Lewis,[1] in 1933, became interested in the treatment of infant vulvovaginitis with the estrogenic hormone, he introduced a form of treatment of this troublesome, but not dangerous, disease which today offers most encouragement.

Estrogenic hormone therapy of infant vulvovaginitis has undergone many changes in its brief existence. Originally, the hormone was administered subcutaneously and intramuscularly in aqueous and ethylene glycol solutions. Success with the administration of the latter was variable, since Huberman and Israeloff[2] obtained five cures in five cases; Goldberg, Minier and Smite seven cures in nine cases; TeLinde and Brawner, one cure in eleven cases; and Witherspoon, no cures in ten cases. The aqueous solution and estrogen in oil were more successful, however, yielding a higher percentge of cures.

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This form of administration, more particularly the oil preparations, require large amounts of the hormone and long periods of administration. Thus, Mazer and Israel[3] use 1,000 rat units of estradiol benzoate hyperdermically every other day for a period of eight weeks, about 28,000 units total; TeLinde[4] uses 800 international units daily for two weeks after negative smears are obtained which averages 17.5 days; and Limper and Hieronymus[2] use 300 rat units twice weekly for four weeks after negative smears are obtained, which requires an initial period of two to four weeks. The results of this form of therapy are excellent as reported by these authors.

The oral administration of the hormone is less satisfactory. TeLinde[4] has used doses of from 3,000 to 16,000 international units for periods of 69-123 days without success. Goldberg[2] has used this mode of administration alone and in conjunction with hypodermic injections with more success. Mazer and Shechter[13] treated three cases unsuccessfully by oral administration of the hormone and finally resorted to other methods. British physicians[5] favor oral administration of estrogen in daily doses of 3,000-6,000 units because of the ease with which children are so managed. In general, however, at least four times the dosage given parenterally is necessary to be effective orally.

The administration of estrogenic hormone by vaginal suppository offers the best prognosis and is least disturbing to the patient. Berger[6] has shown that the hormone may be administered vaginally to adult rats evoking estrus in one-tenth the dosage necessary to produce the same result by the hypodermic route. Hence, this method has been adopted by TeLinde,[4] who has obtained 98 per cent cures, averaging 26.3 days of treatment, using 600 international units daily.

Since the introduction of sulfanilamide in the treatment of gonococcal disorders, attention has been turned to this drug in specific vulvovaginitis. Holmes, Jones and Gildersleeve,[7] Hoffman, Schneider, Blatt and Herrold,[8] Hoberg and Reck,[9] Adler[10] and others have used sulfanilamide in gonococcal vaginitis of children, using doses varying from one-half grain to one grain per pound body weight daily, reducing the dosage with the appearance of improvement. The period of treatment varied from one to sixteen weeks, using continuous or intermittent treatment. Holmes, Jones and Gildersleeve[7] investigated the blood concentration levels of sulfanilamide in their series and found that variation in it of from 0.5 to 9.0 milligrams per cent resulted from daily doses of 0.6 gram per 20 pounds body weight. They decided from their results that the blood concentration level of the drug was no indication of success or failure. Undesirable effects from the drug were mild and of no particular consequence, usually malaise, nausea and anorexia. Neutropenia did not develop in the 139 cases grouped above. The results, as reported by the above named authors, are as follows: Holmes *et al.*,[7] 42 cases, 8 cures, 16 temporary relief; Hoberg and Reck,[9] 50 cases, good results in 28, failure in 13, questionable in 9; Hoffman *et al.*,[8] 25 cases, 18 cures; Adler,[10] 22 cases, 16 cures, although sulfanilamide was supplemented by estrogenic therapy in 3, and 6 failures. Holmes *et al.*[7] used sulfanilamide by suppository, but discontinued this method shortly after discovering marked local irritation without benefit to the original condition.

Friedman and Stettheimer[11] report the death of a child treated for gonococcal vaginitis by means of artificial hyperpyrexia.

The series presented in this paper represents those patients seen in the Hutchinson Memorial Clinic of Tulane University between 1933 and the present, and treated in the departments of gynecology, urology and pediatrics. The age of the patients varied from 23 months to 10 years; over half of them were from 6 to 8 years of age. There was a preponderance of white over Negro, but the clinic population is chiefly white. The diagnosis in every case was considered nonspecific until Gram-negative intracellular diplococci, morphologically gonococci, were found.

DISTRIBUTION OF CASES AS TO THERAPY

Type of Case	Type of Therapy				Total
	Hormone Alone	Other Means Followed by Hormone	Hormone with Adjunct Therapy	Other Means, No Hormone	
Specific	13	3	6	1	23
Nonspecific	1	0	0	2	3
Total	14	3	6	3	26

Table 1

Smears were taken at each visit and a search was instituted for the specific organisms. The relative number of pus cells was estimated, as were bacteria and epithelial cells. The latter were noted, particularly after the hormonal therapy was instituted. The effect of the therapy could be estimated by studying the effect of the hormone on the nuclei of the epithelial cells.

Let us digress for a moment to state the effect of estrogenic hormone on the vagina of infants. As has been well demonstrated by TeLinde,[4] the infant vagina has stratified squamous epithelium of 6-8 cell layers thickness, the surface layer of which is characterized by rounded epithelial cells having ovoid vesicular nuclei. Under the influence of estrogenic hormone, this epithelium progressively thickens, approaching the thickness of adult vaginal mucosa (15-20

Case	G. C.	Age in Years	Total Dosage of Hormone	Duration of Treatment	Recurrence	No. Negative Smears on Discharge	Adjunct Therapy
1	+	9	113,000	21 mon.	Yes	4	$KMnO_4$, mercurochrome, gentian violet throughout treatment
2	+		24,000	3 mon.	No	5	Silver protein instillations for two months prior to hormone
3	+	7	24,000	2 mon.	Yes	4	None
			26,000	1 mon.	No		
4	+	7	28,000	4 wks.	No	4	None
5	—	9	24,000	4 wks.	No		None
6	+	6	24,000	3 mon.	No	4	None
7	+	8		3 mon.	No	4	$KMnO_4$ irrigations, sulfanilamide gr. xv daily for 4 weeks. $AGNO_3$ 10 per cent to cervix
8	+	5	6,000	6 days	Yes	4	Silver protein 10 per cent locally
			12,000	18 days	No		
9	+	9	27,000	9 mon.	Yes	9	$KMnO_4$ irrigations 2 per cent. $AGNO_3$ to cervix
10	+	7	32,000	8 mon.	No	6	$KMnO_4$ irrigations, $AGNO_3$ 20 per cent to cervix
11	—	3	None	7 days			Sulfanilamide gr. xv daily for 6 days. Two per cent gentian violet to vagina
12	+	6	24,000	14 days	No	4	Treated elsewhere previously, having sulfanilamide and douches
13	+	8	36,000	3 mon.	No	4	Sulfanilamide 200 gr. in 10 days
14	+	10	24,000	4 wks.	No	4	None
15	+	6	51,000	5 mon.	Yes	4	Sulfanilamide 150 gr. for 10 days in between courses of estrogen
16	+	8	24,000	4 wks.	No	4	None
17	+	3	24,000	9 wks.	No	4	Formerly treated elsewhere with douches; recurred
18	+	7	69,000	4 mon.	Yes	4	None
19	+	6	24,000	2 mon.	No	4	None
20	+	5	18,000	9 wks.	No	4	None
21	+	8	24,000	5 mon.	No	5	None
22	+	10	18,000	8 wks.	No	6	Treated previously elsewhere 1½ years
23	+	7	18,000	5 wks.	No	4	None
24	+	2	24,000	2 mon.	No	4	None
25	+	6	36,000	2 mon.	No	4	None
26	—	4					Silver protein wicks, $NaHCO_3$ irrigations

Table 2

cell layers). Adult epithelium is cornified and the superficial cells have no nucleus. Contrary to TeLinde, our cases showing the maximum estrin effect continue to show pyknotic nuclei with densely packed chromatin, with an occasional cell without a nucleus. The success of the therapy depends upon such epithelial changes in which glycogen deposits are heavy and whose surface pH is lowered from approximately 7.2 to about 6 or less. Weinstein and Howard[12] have shown a similar change in senile vaginitis and have proven that bacteria play no role in the development of acidity. As TeLinde has demonstrated, acidity alone will not produce the cure, but the epithelial change is of paramount importance. It has been our observation that some few cases (Nos. 13, 14, 16, *Table 2*) were refractory, the epithelial changes requiring more sustained treatment.

The routine of treatment, when the diagnosis of gonococcal vulvovaginitis had been made, was twofold. First, simple cleansing of the vulva twice daily with warm soap and water by the mother was the only local therapy instituted on the gynecologic and pediatric services. On the urologic service this was supplemented with weak potassium permanganate vaginal irrigations in the office at each visit. This, we felt, was of doubtful value, but not harmful. Secondly, suppositories of 1,000 international units were inserted for 18-24 nights. Experience has taught us that 18,000 units may be considered a minimum, and additional dosage added, depending on the effect noticed in weekly vaginal smears. Four negative smears, at least, were required for release from the service, and follow-ups one and two months afterward were made when possible. All cases indicated as relapses (*Table 2*) were given subsequent courses, and all were discharged as cured. Resistant cases were examined for the possibility of a concomitant urethritis, such as was found in one case (No. 13, *Table 2*), which received sulfanilamide as supplementary therapy. In a few cases with small hymeneal openings, it was necessary to pass a Kelly endoscope before the treatment became efficient. Probably the small opening prevented adequate insertion of the suppository. It is also advisable to examine all cases rectally at least once to rule out the possibility of the presence of a foreign body. In studying the smears we also noticed that, as the desired epithelial response was approached, a thick, creamy discharge containing many saprophytic gram-negative micrococci and gram-positive rods supplanted the greenish, excoriating exudate of the disease. Pus cells were characteristically absent or rarely found at this stage. The nonspecific cases ordinarily did not require hormonal therapy, but the case presented (No. 5, *Table 2*) had had a diagnosis of specific vulvovaginitis made at another institution prior to entering ours. Hence, we felt that hormonal therapy should be given in this instance.

The ill effects noticed by hypodermic injections of estrogenic hormone, namely, enlargement of the breast and congestion of the vulva, have not been observed in our series treated by vaginal administration.

CONCLUSION

Gonococcal vulvovaginitis in children is best treated by estrogenic hormone (*Table 3*). The mode of administration may be oral, by hypodermic or suppository. Suppository administration is advisable because (1) it offers the most efficient and most direct action; (2) its ease of administration is an important factor in the treatment of children; (3) the treatment may be conducted by the patient's mother at home with minimal inconvenience to patient and physician. We offer a report of 23 cured cases with

COMPARISON OF SULFANILAMIDE AND ESTROGENIC THERAPY

(I) Sulfanilamide

Author	No. of Cases	Cures	Recurrences	Failure	Ill Effects
Hoffman *et al.*	25	18	0	7	6
Adler	22	16	0	6	7
Holmes *et al.*	42	8	16	18	15
Hoberg *et al.*	50	28	9	13	0
Total	139	70	25	44	28
(II) Estrogenic Suppositories					
TeLinde	159	157	2	0	0
Mazer	34	33	0	1*	8
Author	23	17	6†	0	0
Total	216	207	8	1	8

*Cured by hypodermic administration of estrogenic hormone.
†Cured by a second course of suppositories.

Table 3

adequate follow-up in support of these statements.*

*We wish to express our appreciation to Eli Lilly & Co. for the estrone suppositories used in the majority of the cases presented.

REFERENCES

1. Lewis, R. M.: Amer. Jour. Obst. & Gyn., **26**:593, 1933.
2. Quoted from Limper, M. A.; and Hieronymus, E. E.: Jour. Pediat., **9**:240, 1936.
3. Mazer, C.; and Israel, S. L.: J.A.M.A., **108**:163, 1937.
4. TeLinde, R. W.: J.A.M.A., **110**:1633, 1938.
5. Committee Report. Brit. Med. Jour., **1**:961, 1938.
6. Berger: Abst. J.A.M.A., **105**:2191, 1935.
7. Holmes, J. W.; Jones, J. A.; and Gildersleeve, N.: Jour. Pediat., **12**:610, 1938.
8. Hoffman, S. J.; Schneider, M.; Blatt, M. L.; and Herrold, R. D.: J.A.M.A., **110**:1541, 1938.
9. Hoberg, J. E.; and Reck, L. E.: Ohio State Med. Jour., **34**:1249, 1939.
10. Adler, E. L.: Amer. Jour. Dis. Child., **56**:1424, 1938.
11. Friedman, E.; and Stettheimer, C. J.: Jour. Pediat., **12**: 514, 1938.
12. Weinstein, L.; and Howard, J. H.: Amer. Jour. Obst. & Gyn., **37**:698, 1939.
13. Mazer, C.; and Shechter, F. R.: J.A.M.A., **112**:1925, 1939.

THE USE OF TESTOSTERONE PROPIONATE IN IMPOTENCE: CLINICAL STUDIES WITH MALE SEX HORMONES (III)*

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Impotence is, in each case, a highly individual problem, in which the etiological factors may be simple or complex. The disturbance may affect orgasm, ejaculation, or erection. Weak or incomplete erection may make intromission difficult or impossible. Orgasm may be premature, even preceding intromission, or the orgasm itself may be inadequate as regards sensation and be accompanied by little or no discharge of seminal fluid. Impotence may be purely symptomatic, or may occur as a leading personality difficulty. In each case, one must evaluate the role of possible organic urological disease, hormonal deficiency, interference with the nervous pathways, psychological or personality factors, or a combination of disturbances in all four fields. Thus the diagnosis and treatment of impotence requires the joint cooperation of the urologist and the psychiatrically trained physician. The former is apt to rely largely on organic methods, such as prostatic massage, cauterization, etc. The psychiatrist must begin his treatment with an adequate knowledge of the urological, endocrine and medical status.

Often certain minor genito-urinary abnormalities, such as changes in the verumontanum or prostatic urethra, are the result rather than the cause of the condition, and it is known that such pathologic changes may exist, even to the point of bloody ejaculation, without any effect whatever on the sexual potency of the individual.[1] As early as 1894, Steinach[2] showed that animals were able to copulate after removal of the prostate and seminal vesicles. One of us (S.A.V.) has observed the complete preservation of the erection and orgasm in two patients after radical perineal prostatectomy, in which the entire prostate, seminal vesicles, ampullae of the vasa, and vesical orifice were removed *en masse*. On the other hand, we have observed complete loss of potentia after removal of a single seminal vesicle. Such observations, together with the well-known capacity of erection in some postpubertal eunuchs, makes the evaluation of the urologic findings exceedingly difficult. Thorough physical examination is necessary to rule out infectious inflammatory conditions, new growths, prostatitis, and so on. Neurologic and toxic factors such as excessive use of alcohol, drugs or nicotine, must be excluded. Psychiatrically, states of depression, early schizophrenic conditions, or cerebral lesions must be excluded or, if present, given consideration in treatment. We must remember, also, that certain factors disturbing the normal physiologic functions may play a role, such as too frequent intercourse, general fatigue and debility, the use of contraceptives, coitus interruptus, periods of abstinence, and so on. Difficulties of the newly married, springing from inadequate information concerning the technic of intercourse, and fear of difficulty, resistant hymen, small vaginal outlet, improper lubrication, can play a role and may be amenable to simple explanation and reorientation. If neglected, these factors may lead to frigidity in the woman, and the resulting incompatibility sometimes leads to impotence.

A large group of cases, however, is essentially psychogenic in origin and arises from factors in the individual personality make-up which must be carefully understood and corrected before treatment can become effective. Such a

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study seeks to make clear the actual amount of physiologic sex drive present as a basis for reorientation. Many factors in the life development may play a role: prolonged sexual excitement without orgasm, apprehension and fear of failure, excitement of anticipation, sexual misinterpretations and misinformation. Sometimes impotence may be the result of general insecurity and anxiety engendered by other situations in life, such as financial loss, occupational strain or worry. There are other cases, however, in which the difficulty may be rooted much more deeply in the personality, and such factors as latent or overt homosexuality and bisexuality, anal-erotic, sadistic and narcissistic features create a vastly more complex and sometimes unmodifiable problem. Deep-seated inadequacy may spring from fear of intercourse, castration fears, fear of venereal disease, feelings of inadequacy based on organic defects such as varicocele or undescended testicle.

A careful scrutiny of the entire sexual development is necessary in order to clarify specific factors which are at fault in any individual patient. Much can be done psychotherapeutically if the patient puts all the facts before the physician and is able to recreate the steps in the development of his difficulty so that reorientation can be achieved. Re-establishment of confidence is imperative, and various psychiatric methods such as explanation, reassurance, persuasion and hypnosis have proven effective.

The question arises whether in those individuals with psychogenic impotence an increase in the amount of sexual urge might be produced by hormonal medication, which would thereby increase the confidence of the impotent male to the extent that he might overcome his difficulty. At the outset it should be stated that the evaluation of the presence or absence of adequate male sex hormones in the body is at present very crude and is not in our opinion determined satisfactorily by urinary hormone assay. Except in the aged, the best criteria still seem to be the status of the secondary sex characteristics, namely, size of penis, prostate, seminal vesicles, the status of the body hair, and voice. Even these objective signs cannot readily disclose minor variations from the normal. We had clearly in mind that in most cases of impotence the physiological mechanism is intact, as proved by the presence of erection during masturbation, occasionally with another partner in extra-marital relations, in erotic dreams, morning erections, and nocturnal emissions. Fifteen cases of impotence were selected for joint medical, urologic and psychiatric study. The medical, urologic and psychiatric examiners had in each case come independently to the conclusion that the patients represented cases of psychogenic impotence. Neither genito-urinary nor medical examination revealed any basic organic condition. By objective study there was no indication for assuming any hormonal deficiency in any of the patients. Only eight cases were selected for testosterone therapy, the others being excluded either because it was felt that their problems were too deeply rooted in fundamental personality difficulties, or because the patients were inaccessible for systematic therapy. The eight cases utilized were as follows:

A. G., a 34-year-old married man, complained that since the age of 19 he had had no real satisfaction from intercourse. He was capable of carrying out the act with his wife, but experienced little sensation and no pleasure. He felt that masturbation, which began at 13, exhausted his passion, because it was often excessive and accompanied by abnormal fantasies. He denied ever having a nocturnal emission. From childhood onward he was shy, timid, bookish, passive, unsuccessful. At present he had constant fatigue, anxiety and depressive symptoms. He had been unable to hold a job. He was given 25 milligram injections of testosterone propionate three times a week until he had taken 36 injections, or 900 milligrams. No change in his sexual, general mental, or physical status resulted. There were no spontaneous erections, nocturnal emissions, nor any stimulation or change in sensation during coitus. No change in the size of the prostate, seminal vesicles or testes was observed.

V. K., a 43-year-old, unmarried, intelligent man, complained of infrequent and unsustained erections. Orgasm was without ejaculation. A few attempts with prostitutes were partially successful, but he had considerable difficulty in maintaining adequate erection. He lost confidence in his capacity. Masturbation was practiced for relief. As a child he was shy, timid, easily frightened, had many neurotic traits and was sensitive about his small penis. Masturbation as his usual outlet caused considerable conflict with his rigid Catholic background. Nocturnal emissions occurred once a week. He was given 25 milligram injections of testosterone propionate three times per week for a total of 10 injections. No alteration in his status, either subjective or objective, was noted.

C. D., a 43-year-old widower, complained of inability to maintain an erection long enough to accomplish satisfactory intercourse. The erection would subside either immediately before or after entrance, and ejaculation was premature. The difficulty was present temporarily at the beginning of his marriage, but corrected itself. Since his wife's death eight years ago he had attempted intercourse persistently with his paramour, but without success. He had become discouraged and feared to attempt sex relations. Even during masturbation he lost the erection before ejaculation. Nocturnal emissions occurred twice monthly, but never with erection. He was a worrier, sensitive, easily embarrassed, conscien-

tious, anticipatory, and a man of limited intelligence. Active psychotherapy and later topical applications to the posterior urethra failed to improve his status. He was given 25 milligrams of testosterone propionate three times a week for two weeks without any evidence of stimulation.

D. G., a 47-year-old widower, complained of inability to achieve erections. This difficulty had been present occasionally prior to 1925. He was greatly improved following thyroidectomy for three years, until his wife's death, when his difficulty recurred. He forced himself to attempt intercourse, with failure most of the time. He had a naturally slow sex pace, which he attempted to speed up. He was dissatisfied with his work and saw no future for himself. He was self-conscious, easily embarrassed, at ease rarely, and was often morose and despondent following sexual failures. He dreaded each new sexual encounter because he anticipated failure. Nine injections of 25 milligrams of testosterone propionate, given over a period of three weeks, resulted in no change, either subjectively or objectively.

E. S., a 47-year-old unmarried man, gave a story of lifelong masturbation which he felt had damaged him mentally, producing poor concentration, poor memory, and a sense of devitalization. Attempts at intercourse resulted in incomplete erection and premature ejaculation. He was a man of limited intelligence, with schizophrenic delusional convictions of the harm he had done himself. Urologic treatment to the posterior urethra and prostatic massage failed to benefit him. He was given 25 milligram injections of testosterone propionate every other day for two weeks, without any improvement in the rigidity of the penis, increase in frequency of erections or change in the premature ejaculations.

F. A., a 59-year-old married man, complained of lifelong premature ejaculation which he attributed possibly to sexual extravagance. While he sought sexual encounters about twice a week as a youth, he frequently had intercourse six or eight times a night. At 31, following a protracted relationship with an actress, with whom he had frequent intercourse, he found, for the first time, that he could not get an erection. Four years later the seminal vesicles were drained through the perineum, and for six months after he showed improvement. Again intermittent impotence occurred. At 46, he married, but for the previous four years there had been a dwindling libido toward his wife, and if the sexual act was at all prolonged, his erection disappeared. Intercourse was easier under the influence of alcohol, when he lost his apprehension. In the preceding two years he had had endoscopic treatment and prostatic massage, without benefit. Physical examination showed only early benign prostatic hypertrophy. He was given 18 injections of testosterone propionate three times weekly and reported: "The medication has been not merely negative, but detrimental, having produced a result diametrically opposite to what I had hoped."

G. G., a 36-year-old married man, complained of inability to maintain an erection and of the production of very little fluid on ejaculation. These symptoms had been present since his first intercourse at the age of 19, when he noticed that orgasm brought the ejaculation of very little semen. Intercourse was sometimes pleasurable, sometimes painful, but he had usually only partial erection at the time of ejaculation. Masturbation began at the age of 17 and, on one occasion, was performed by another boy, which occasion was the only time in his life that he had an adequate production of seminal fluid. He complained also of "spells" present since the age of 8, with probably major epileptic convulsions rarely, but frequent *petit mal* attacks. He was greatly concerned about this, feared to go to sleep because the attacks came just preceding sleep. They were increased by excitement and worry. He felt confident that if the spells could be eliminated the sexual difficulty would correct itself, since he was convinced that the two were dependent upon each other. He was a man of limited intelligence, with a tendency to worry, brooding over his own condition, and his impotence was probably associated with worry and anxiety concerning the *petit mal* attacks. He had had gonorrhea at 23. Examination revealed a scar at the site of a congenitally imperforate anus, osteoarthritis of the spine and mild chronic prostatitis. In February, 1937, plication of the bulbo- and ischio-cavernosus muscles was performed with slight temporary improvement. Following six daily injections of 25 milligrams of testosterone propionate he thought there was slight improvement in erection. There were, however, several failures at intercourse. A second series of seven daily injections was given. He reported very slight improvement in sexual function, but reported also that he had no faith in the therapy and clung to the belief that if his seizures could be eradicated his sexual potency would return.

H. J., a 28-year-old unmarried chauffeur of limited intelligence and farm background, complained of sexual weakness, lifelong premature ejaculation and, in the past three years, only partial erections, which made penetration impossible. Masturbation began at 16, was continued for a year and given up because he feared it would wreck his health. Intercourse began at 17 years. In the past three years he had never had an adequate erection, even on waking in the morning or with daydreams. At the time of examination, emission occurred with partial erection, but gave no pleasure. He wanted cure, because "if I get all right, I plan to be married." Throughout his life he had been nervous, embarrassed, flushed easily, became easily exhausted and had a definite neurasthenic condition. He was the youngest of three children, attached to his mother, and had lived at home until a year previously. He was ill at ease with people and had never been a leader. He had just managed to get through high school and did farm work for his father until exhaustion led to change of employment three years previously. He was ambitious, lacked confidence, and presented a picture of lifelong constitutional inadequacy and make-up, of which the sexual inadequacy was one part. Many therapies had been tried, including prostatic massage and pituitary extracts. Testosterone propionate, 25 milligrams three times weekly for six weeks, produced absolutely no improvement.

In the ninth case, testosterone propionate was used to see its effect on a homosexual patient who suffered with general symptoms of fatigue and nervousness:

J. H., a 23-year-old, single homosexual, complained of obesity, fatigue, tension and poor concentration. There was one protracted, overt relationship. Nocturnal emissions occurred once a month, leaving him tired and less efficient the next day. He showed no desire to become heterosexual. Twelve injections of 25 milli-

grams of testosterone propionate, given three times per week, produced no effect on any of his symptoms.

It seems unlikely that male sex hormones will change the direction of the libido in an overt homosexual whose amount of libido is normal, but in whom the channel of expression is diverted.

Numerous observations have been made to the effect that libido and potentia can be produced in castrates and prepubertal animals by the administration of androgens.[3] Crystalline male hormones have provoked erections in immature monkeys and infants,[4] masturbation in a 4-year-old boy[5] and marked libido and potentia in hypogonad patients.[5 6 7 8 9] In our experience, administration of 25 milligrams of testosterone propionate twice weekly to hypogonad patients has invariably been followed by signs of sexual stimulation within the first two weeks.[6] But in a few normal young adult male volunteers these doses or, in fact, twice these doses, have resulted in no signs of increased sexual urge whatever. These observations suggest that the clinical response to male hormones is more vigorous in patients with hormonal deficiency than in the normal. To some elderly patients suffering with prostatic hypertrophy we have given similar doses of testosterone propionate. In one or two instances increase of erections and return of libido have occurred. We have felt that in all probability the patients so responding suffered from deficiency of internal testicular secretion.

With less detailed studies than in the nine patients reported above, we have treated approximately 50 other impotent patients with testosterone propionate, the impotence resulting from a wide variety of causes. We have observed no instance of sexual stimulation as a result of this therapy except in one or two elderly patients, in whom deficiency of male hormone may well have been a factor.

Hamilton,[4] Schmitz,[10] Miller, Hubert and Hamilton[11] have reported good results in psychic impotence from androgenic hormone therapy. The instances in the literature, alluding to the value of androgenic therapy in psychic impotence, have not been published in sufficient detail for us to rule out the factor of hormonal deficiency in their etiology or the factor of suggestion in their cure. In our own cases we are satisfied that no gross hormonal deficiency existed. As we have pointed out previously,[8] the element of suggestion must be given great consideration in evaluating the efficacy of any therapy for impotence.

It is our impression, therefore, that unless hormonal deficiency exists, there is little likelihood that any stimulation will result from androgenic therapy, at least in doses of the order of magnitude which would produce such effects dramatically in hypogonad patients. We can, however, see no harm in giving the material a therapeutic trial in questionable cases.

We have seen no ill effects from the use of testosterone propionate either in normals or in impotent patients. It has been suggested that the drug may cause sterility by reducing the hypophyseal gonadotropic hormone secretion. One of our hypogonad patients[5] had been married eight years prior to his testosterone propionate therapy, and the marriage had been sterile. Since treatment in the past two and a half years there have been two pregnancies, and a recent sperm count on the patient's ejaculate is found to be 150 million.

SUMMARY

Among 8 cases of psychic impotence, treated with injections of testosterone propionate, none reported improvement. No change in symptoms was noted in a male homosexual patient similarly treated. If the factor of suggestion is ruled out it seems unlikely to us, in spite of other reports, that in states of psychic impotence specific male hormones in doses adequate for excellent responses in hypogonad patients offer any therapeutic help.

BIBLIOGRAPHY

1. Hohman, L. B.; and Scott, W. W.: Combined Psychiatric and Urologic Study of Sexual Impotence. Jour. Urol., **29**:59-76, 1933.
2. Steinach, E.: Untersuchungen zur der gleichenden Physiologie der mannlichen Geschlechtsorgane insbesondere der accessorischen Geschlechtsdrusen. Pfluger's Arch. f. d. ges. Physiol., **56**:304-338, 1894.
3. Shapiro, H. A.: Effect of Testosterone Propionate on Mating. Nature, London, **139**:588-589, 1937.
4. Hamilton, J. B.: Induction of Penile Erection by Male Hormone Substances. Endocrinology, **21**:744-749, 1937.
5. Vest, S. A., Jr.; and Howard, J. E.: Clinical Experiments with the Use of Male Sex Hormones. (I) Jour. Urol., **40**: 154, 1938.
6. Hamilton, J. B.: Treatment of Sexual Underdevelopment with Synthetic Male Hormone Substance. Endocrinology, **21**:649-654, 1937.
7. Kenyon, A. T.: Effect of Testosterone Propionate on Genitalia, Prostate, Secondary Sex Characteristics and Body Weight in Eunuchoidism. Endocrinology, **23**:121-134, 1938.
8. Howard, J. E.; and Vest, S. A., Jr.: Clinical Experiments with the Use of Male Sex Hormones. (II) Amer. Jour. Med. Sci., in press.
9. McCullagh, E. P.: Treatment of Testicular Deficiency with Testosterone Propionate. J.A.M.A., **112**:1037-1044, 1939.
10. Schmitz, G.: Erfahrungen mit dem neuen synthetischen Testeshormonpraparat "Perandren." Deutsche med. Wchnschr., **63**:230-231, 1937.
11. Miller, N. E.; Hubert, G.; and Hamilton, J. B.: Mental and Behavioral Changes Following Male Hormone Treatment of Adult Castration, Hypogonadism and Psychic Impotence. Proc. Soc. Exper. Biol. & Med., **38**:538-540, 1938.

THE TREATMENT OF CANCER OF THE LARYNX WITH COMPARISON OF RESULTS OBTAINED BY SURGERY AND RADIATION THERAPY*

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Cancer occupies place number two[1] in the list of causes of death in the United States. Of the total cancer deaths that of the larynx constitutes about 1.8 per cent.[2] Laryngeal cancer, if properly diagnosed and treated, is curable in a very high percentage of cases, and yet "the majority of individuals with cancer of the larynx die from cancer of the larynx."[3] The statement that cancer of the larynx is curable is the result of more or less recent developments. Sir St. Clair Thomson quotes Morell Mackenzie, who said as recently as 68 years ago: "The only possible termination of cancer is death," and J. Nolan Mackenzie, his assistant, wrote in 1879 that "there was never a thought of cure." The history of the treatment of this disease since then describes the great and numerous disappointments with the periods of hope and despair through which surgeons have passed in their efforts to achieve something in the way of satisfactory treatment of this disease. The literature is filled with accounts of the experience of surgeons all over the world bearing out these facts. Sir St. Clair Thomson, in his book "Cancer of the Larynx," has presented the historical data pertaining to this subject in a most charming and interesting manner.

In selecting treatment certain facts seem well established, namely: the need for early diagnosis and prompt treatment; clinical classification as to location and extent; microscopic classification or cell typing; consideration of the patient's general health and possible metastases. The location of the cancer has a most important bearing on the type of treatment to be recommended. Cancer of the true cord is a strictly localized disease, while no other laryngeal cancer may be said to be localized.

Up until well within our time the method of destroying cancer of all varieties was surgical in some form. Then with the discovery of its possibilities radiation therapy has assumed, and very properly, too, a position of great importance in the treatment of cancer in all regions of the body, including the larynx. The situation today is that there are many brilliant workers who feel that radiation therapy is adequate and preferable for all forms of cancer, early or late. This in spite of the statement of Douglas Harmer,[4] who speaks from large experience regarding radiation therapy, that "At present there is certainly no agreement as to the best method of giving rays." But there is an equally brilliant and well seasoned group who feel that surgical approach, including diathermy or other methods of destruction by heat, is the treatment of choice, especially for early cancer, reserving the use of radiation therapy for those cases which are inoperable. And then we find a group who prefer surgery and radiation therapy combined. Since, as you all know, it is impossible for any one group to show results entirely satisfactory to themselves or others, it is difficult for the man in the street to make up his mind as to which is the treatment to be preferred. It is my feeling that the treatment should be selected to fit the requirements of the case in each instance. Many men of experience agree with Sir St. Clair Thomson, who says that in true cordal cancer treated by laryngofissure we may expect in over 80 per cent of cases a lasting cure without loss of function. Our experience bears out the truth of this statement. In all other types of laryngeal cancer laryngectomy with gland dissection will obtain lasting cure in a much smaller group of cases, but with mutilation and with the well grounded fear of recurrence and metastases. Radiation in addition to laryngectomy and gland dissection increases the possibility for cure. After laryngofissure the operative mortality rate is practically nil, whereas after laryngectomy it is comparatively high.

As for radiation therapy alone, we do not find reported results of treatment of cordal cancer by this method which equal the results obtained by surgical removal. In other types of laryngeal cancer with lymphatic involvement, the results obtained by radiation therapy alone are better than those obtained by surgical treatment. It is highly probable that with continued improvement in technic of administration radiation therapy may become the universal method of choice

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for treating extrinsic cancer of the larynx and possibly for intrinsic cancer as well.

Many individuals, both lay and medical, have the mistaken idea that the suffering, mutilation and actual danger to life resulting from surgical intervention is much greater than that from radiation therapy. No idea was ever further from the truth. Particularly does this apply when radiation therapy is administered to the syphilitic or to the aged and infirm.

Because of the great volume of material in the current literature, it is impossible to quote or even to refer to all the material now available. I have therefore selected for inclusion in this report a few statements from men throughout the world whose opinions, because of their tremendous experience, are generally accepted as authoritative.

In a recent communication, Gordon B. New states that his paper[5] in 1932 presents his views up to now on the selection of treatment for carcinoma of the larynx. In this comprehensive article one important statement is: "The objective of educational measures among physicians and the laity should be to bring the patients for consultation early enough so that laryngofissure or thyrotomy could be employed. * * * The results in the surgical treatment of cancer of the larynx demonstrate that operation followed by roentgen rays or radium offers the best method of combating the disease." He leaves the inoperable cases for irradiation without surgery. He stresses the importance of microscopic grading both as an aid in determining the best treatment and in arriving at a prognosis.

Harmer and Finzi,[6] in 1930, in discussing the value of radiation therapy in the treatment of cancer refer back to the experiences of Sir Frederick Treves and Sir Henry Butlin, the first of whom in about 1909 startled the medical profession by stating that "Epithelioma of the tongue and lip are cured by radium." The latter, among other things, stated that "Radium a year ago was in quite an experimental stage in the treatment of epithelioma," and still expressed doubt as to its value. As a result of their experiences at St. Bartholomew's and elsewhere Harmer and Finzi, after discussing the use of this remedy, decided that with smaller doses and better technic their results have steadily improved. After reporting very favorable results from the treatment of intrinsic as well as extrinsic cancer of the larynx by radiation therapy, they say: "It is possible that radium will be found to be the best treatment in all cases of intrinsic carcinoma of the larynx, but it must be remembered that very good results have been obtained by surgery. Undoubtedly, as Butlin has stated, this is a 'very weighty question.' * * * Having studied the results obtained by the two methods and having fully realized the responsibilities of deciding between them, we have come to the conclusion that radium is the best treatment for all cases." This is an extremely interesting and instructive article and should be studied by all interested in the treatment of cancer of the larynx.

In 1934, Douglas Webster,[7] in commenting on his experience in the treatment of cancer of the larynx by the protracted fractional x-ray method of Coutard, says: "In my outlook on x-ray treatment of cancer of the larynx I find I have passed through five or more alternating phases of hopefulness or discouragement. * * * There is no doubt that we are now at the beginning of a really great advance in x-ray therapy." He pointed out the value of smaller doses over longer time. Mr. Douglas Harmer, in discussing this paper, describes his experience in 178 cases of advanced type of cancer of the throat, all inoperable and all late, and says he thinks the treatment will have to be more protracted.

Lionel Colledge,[8] in 1931, points out the beautiful results obtained by surgical intervention. In this article he does not mention treatment by irradiation. Then, in the *British Medical Journal* of 1938, he[9] still feels that as general treatment surgical intervention is preferable, but does point out that carcinoma and Group IV epitheliomas in particular give uniformly bad results with surgery and are radiosensitive.

Fielding O. Lewis,[10] in 1933, made the statement that "the surgical treatment (laryngofissure) in early intrinsic cancer of the larynx yields more striking and lasting results than can be claimed in any other internal region of the body. About 80 per cent cures is the reported result of experienced operators."

Diggle and Hamilton[11] make the plea that laryngologists publish all cases for the sake of progress in the treatment of this disease. They also urge the necessity for closer cooperation between the laryngologist, the pathologist, and the radiotherapeutist.

Max Cutler[12] calls attention to the value of the Coutard technic in the treatment of cancer of the tonsil, pharynx, and larynx.

Hayes Martin[13] says, in discussing selection of the method of treatment: "In our opinion no single method is suited to the treatment of all the clinical forms and histological varieties of this disease: in some surgery; in others radiation; and in still others a combination of surgery and radiation."

Martin and McNattin[14] say: "It would be of great interest and practical value if one could definitely state the cause of failure in all the unsuccessful cases. The histological findings, in many instances, give no clue."

Simon Jesberg[15] says: "Coutard's treatment offers a definite hope of cure in extrinsic laryngeal cancer and is the treatment of choice to date. Whether or not its use in intrinsic cancer will replace surgical treatment can be answered only by the test of time."

Looper,[16] of Baltimore, favors surgery.

Lars Edling[17] reports primary results in the use of teleradium and says: "The future will show the value of this remedy."

And finally Henri Coutard,[18] in an article entitled "The Conception of Periodicity as a Possible Directing Factor in the Roentgentherapy of Cancer," emphasizes the urgent need for the very closest collaboration between the laryngologist and the radiologist for the purpose of observing the cellulicidal effects of roentgen rays on the normal as well as on the neoplastic cells and in addition the effect of radiation on the patient's general health. He deals at length with the fact that the radiocellulicidal effects on the healthy as well as the

neoplastic cells are periodic and that the treatment must be gauged and guided by the occurrence of the cellulicidal effects. He describes the difference in radiosensitivity in undifferentiated and differentiated cancers and shows in his table the proportion of successful cases in the one group as against the unsuccessful in the other. Again in September, 1937, this author[19] reports results of treatment and lays emphasis upon the vast difference in results obtained by radiation therapy of cancers made up of undifferentiated cells and of cancers made up of differentiated cells. He also stresses the importance of recognizing two general forms of roentgen therapy, namely, quantitative and qualitative.

I have asked some of my friends abroad to give me the benefit of their experience with treatment of cancer of the larynx. Their responses are herewith quoted.

From Mr. V. E. Negus, of London, England, October 31, 1938: "I really think the remarks I made at Atlantic City sum up the views I have formed here about the treatment of cancer of the larynx. They can be condensed as follows:

"(1) Growth of Group I or II limited to anterior half of one cord: laryngofissure.

"(2) Extensive growth right along one cord reaching posterior commissure: interstitial radium with needles.

"(3) Growth on one cord just reaching arytenoid, rather extensive for removal, Group I or II, laryngofissure; Group III or IV, interstitial radiation.

"(4) If patient is unsuitable for operation, or refuses it, teleradium is used instead of interstitial radium.

"(5) Growth of low grade malignancy, intrinsic type affecting anterior ends of both cords, anterior hemilaryngectomy.

"(6) Growth of low grade affecting both cords and spreading to posterior commissure, total laryngectomy.

"(7) Growth of high grade malignancy affecting both cords extensively, teleradium.

"(8) Secondary glands, if not fixed, can be removed by block dissection.

"It is difficult to decide in certain cases, but these are the lines I should take."

Dr. Ewart Martin, of Edinburgh, Scotland, thinks that in early extrinsic carcinoma of the larynx excision of the larynx is proper. He does not think that radium or x-ray treatment is of any use when the carcinoma is extrinsic; but he remarks further: "Unfortunately many of these cases are hopeless before we see them, and then one has to try deep x-ray treatment or the implantation of radium, but without much hope of success." In cordal cancer he thinks removal of the cord through laryngofissure is the ideal method and quotes cases observed as long as fourteen years after operation without recurrence. He furthermore quotes the late Dr. J. S. Fraser, who referred to a series of cases which had been operated upon by the Finzi-Harmer technic of window resection of the thyroid and then use of radium. He reported no recurrences and a perfect voice in each case. He states that experiences here have varied. "I have had the bad luck to have 3 cases of perichondritis of the cartilage; one on the same side and the other two on the opposite side. In one case the perichondritis came on six months after implantation of the radium, and the other two cases within a year." He has also seen two other cases develop perichondritis two years after operation. "This occurrence makes one think a little before using radium in preference to laryngofissure. * * * We have had little experience with deep x-ray therapy as a primary treatment, but have used it where there has been a recurrence after radium."

I am reporting a short series of cases which I have seen in the wards of the Barnes Hospital, the Washington University Dispensary, and in my private practice. Radiation therapy in one case of this group was prescribed by Dr. L. R. Sante at the St. Louis City Hospital. In all the others it was prescribed by Dr. Sherwood Moore, Dr. Wendell G. Scott, Dr. A. N. Arneson, or Dr. Oscar Zink, of the Mallinckrodt Institute of Radiology. As may be seen from the chart, the series includes 34 cases of carcinoma of the larynx, of which 12 are intrinsic and 22 are extrinsic.

TYPICAL INTRINSIC CASE

C. B., a white man, aged 40, was referred to me in August, 1934, by Dr. Nowlin Holcomb, of Muskogee, Oklahoma, because of hoarseness which had lasted for about eight months. He had consulted several physicians without relief. Dr. Holcomb realized the danger of possible cancer and sent him promptly.

When I saw him, laryngeal examination disclosed the

RESULTS OF TREATMENT IN 34 CASES OF CANCER OF THE LARYNX

INTRINSIC CANCER OF THE LARYNX, 12 CASES
TREATED BY LARYNGOFISSURE, 11 CASES

Nine living. No recurrence over average period of 3 1/3 years, the longest being 10 years and the shortest being 1 year.

Two died from other causes at 4 years and at 7 months, respectively.

TREATED BY LARYNGOFISSURE AND RADIATION THERAPY, 1 CASE

Still living. No recurrence after 2 years and 10 months.

* * * *

EXTRINSIC CANCER OF THE LARYNX, 22 CASES
FIVE TREATED SURGICALLY ONLY

Two died postoperatively.
One lived 3½ years, died of recurrence.
Two lived 1¼ years, died of recurrence.

THREE TREATED BY SURGERY AND RADIATION

One still living, 5 years, no recurrence.
One lived 4½ years, died of recurrence.
One lived 6 months, died of recurrence.

FOURTEEN TREATED BY RADIATION THERAPY

Two living. No recurrence 8 years and 6 months, respectively.

Five lived from 3 months to 1½ years. Died of recurrence.

One lived 1 year and 2 months. Died of sepsis and syphilis.

Two lived 10 months. One died of radiation necrosis and one of metastases.

Four are now under treatment.

Table 1

ANALYSIS OF AUTHOR'S CASES

INTRINSIC CANCER OF THE LARYNX

	Total	Dead	Lost	Alive	Alive Without Disease Years						Dead from Other Causes Years						Dead from Recurrence Years						Still Under Treatment (Months)	
					—1	1	2	3	4	5	5+	—1	1	2	3	4	5	5+	—1	1	2	3	4	5	5+	—6	6
Treated by laryngofissure	11	2	—	9	—	2	—	2	3	—	2	1	—	—	—	1	—	—	—	—	—	—	—	—	—	—
Treated by laryngofissure and radiation	1	—	—	1	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Total	12	2	—	10	—	2	1	2	3	—	7	1	—	—	—	1	—	—	—	—	—	—	—	—	—	—

EXTRINSIC CANCER OF THE LARYNX

	Total	Dead	Lost	Alive	Alive Without Disease Years						Dead from Other Causes Years						Dead from Recurrence Years						Still Under Treatment (Months)	
					—1	1	2	3	4	5	5+	—1	1	2	3	4	5	5+	—1	1	2	3	4	5	5+	—6	6
Treated by laryngectomy	5	5	—	—	—	—	—	—	—	—	—	2	—	—	—	—	—	—	—	2	—	1	—	—	—	—	—
Treated by surgery and radiation	3	2	—	1	—	—	—	—	—	—	1	—	—	—	—	—	—	—	1	—	—	—	1	—	—	—	—
Treated by radiation only	14	8	—	6	1	—	—	—	—	—	1	2	1	—	—	—	—	—	4	1	—	—	—	—	—	3	1
Total	22	15	—	7	1	—	—	—	—	—	2	4	1	—	—	—	—	—	5	3	—	1	1	—	—	3	1

Table 2

fact that he had a grayish mass in the middle third of the left vocal cord stopping short of the anterior commissure and not extending beyond the vocal process posteriorly.

The clinical diagnosis of cancer was confirmed on biopsy study, with the statement that the cells were well differentiated with pearls and little evidence of mitosis.

Two days later laryngofissure according to St. Clair Thomson's technic was done. The patient developed a granuloma a few months later, which was removed and examined microscopically.

The patient is well and carrying on with his duties as an officer in the National Guard. He has no evidence of recurrence, no respiratory difficulty, and although his voice is husky, he carries on his usual duties without much difficulty. His voice can be heard distinctly across a large lecture hall.

The results in this case are in striking contrast with those obtained in the other case of this series reported in detail.

TYPICAL EXTRINSIC CASE

F. S., a white man, aged 56, was first seen September 18, 1935. His chief complaint was hoarseness for two years, dyspnea, cough, and expectoration for two weeks. His general health had been good except for a stroke seven years previously. At the present time he was in distress because of laryngeal obstruction. His voice was reduced to a whisper. His blood pressure was 160/100.

The history was that two years before he had continued hoarseness, for which he consulted a laryngologist, by whom he was told to see me for diagnosis of his laryngeal disorder. He went back home and talked with his family physician and was advised by him that he would get well if he took cough medicine. After several months on this treatment he became discouraged and quit all treatment. Later he consulted another throat specialist, who in turn advised him to see me. When I saw him he had laryngeal obstruction caused by a tumor mass which occupied the entire right half of the larynx and filled the glottic chink.

There was complete fixation of the right half of the larynx.

Immediate tracheotomy was necessary. The clinical diagnosis of cancer was confirmed on biopsy study. The pathologic diagnosis of the biopsy specimen was squamous cell carcinoma. A laryngectomy was done with lymph node dissection. One gland showed squamous carcinoma.

He developed within two months multiple metastases of the trachea to the bifurcation, which failed to respond to radiation therapy. He died six months after his laryngectomy from general carcinomatosis.

This case is an example of delayed diagnosis and of the almost hopeless outlook from the beginning in a case in which the glands of the neck are widely involved, as was true in this instance.

SUMMARY AND CONCLUSIONS

(1) Cancer occupies second place in the list of causes of death in the United States. Cancer of the larynx constitutes about 1.8 per cent of these.

(2) The site of origin of cancer of the larynx most often is the true vocal cord.

(3) The lymphatic supply to the true vocal cord is practically nil,[20] therefore metastases do not occur while the tumor is still actually confined to the true cord. For the above reason surgical removal by laryngofissure, when the cancer is truly cordal, with lasting cure and without loss of function, is possible in over 80 per cent of cases.

(4) The suffering and inconvenience to the patient after laryngofissure is comparatively little and the mortality rate is very low. Reported results of treatment of cordal cancer by radiation alone do not equal those obtained by surgical treatment.

(5) In extrinsic cancer the results of treatment by radiation alone have, in the last ten years, shown tremendous improvement both in palliation and in cure. With further improvements in technic of administration, I feel that we may confidently expect still greater developments. It is my belief that this is the treatment of choice either alone or combined with surgical approach in this type of cancer.

(6) Treatment must be selected to meet the particular requirements of each case.

(7) The universal cry is for early diagnosis and treatment. The universal practice, almost, is late diagnosis and delayed treatment.

(8) This situation will be corrected and the mortality rate from laryngeal cancer decreased if and when the medical profession as a whole becomes actively aware of these facts.

BIBLIOGRAPHY

1. U. S. Bureau of the Census Report for 1935.
2. Thomson, Sir St. Clair; and Colledge, Lionel: Cancer of the Larynx. Preface, p. 7. Kegan Paul, Trench, Trubner & Co., Ltd., London, 1930.
3. Jackson, Chevalier: Cancer of the Larynx: Its Treatment by Laryngofissure. Sou. Surgeon, **1**:223-229, 1932-1933.
4. Harmer, W. Douglas: The Relative Value of Radiotherapy in the Treatment of Cancers of the Upper Air Passages. University of London, Simon Lecture, 1931. Murray, London, 1931.
5. New, Gordon B.; and Fletcher, Eleanor: The Selection of Treatment for Carcinoma of the Larynx. J.A.M.A., **99**: 1754-1758, 1932.
6. Harmer, Douglas; and Finzi, N. S.: Radium Treatment of Intrinsic Carcinoma of the Larynx. Practitioner, **124**:16-31, 1930.
7. Webster, J. H. Douglas: The Protracted Fractional X-Ray Method (Coutard) in the Treatment of Cancer of the Larynx. Proc. Royal Soc. Med., **27**:901-924, 1933-34.
8. Colledge, Lionel: Operative Treatment of Cancer of the Larynx. Practitioner, **124**:32-40, 1931.
9. Colledge, Lionel: Irradiation for Carcinoma of Oropharynx. Brit. Med. Jour., p. 167, July 23, 1938.
10. Lewis, Fielding O.: Laryngeal Cancer: Statistical Report on Five-Year Cures. Surg., Gyn. & Obst., **56**:466-476, 1933.
11. Diggle, F. H.; and Hamilton, E. S. B.: Laryngeal Malignant Disease and Radium. Jour. Laryng. & Otol., **46**:37-43, 1931.
12. Cutler, Max: Radium Dosage and Technic in Carcinoma of the Tonsil, Pharynx and Larynx. Amer. Jour. Roentgenol. & Rad. Ther., **33**:690-693, 1935.
13. Martin, Hayes E.: The Treatment of Cancer of the Larynx. Trans. Amer. Acad. Ophth. & Otolaryngol., pp. 213-268, 1936.
14. Martin, Hayes E.; and McNattin, Robert F.: The Treatment of Cancer of the Pharynx, Tonsil and Extrinsic Larynx by Divided Doses of External Radiation. Amer. Jour. Radiol. & Rad. Ther., **32**:717-729, 1934.
15. Jesberg, Simon: An Evaluation of Radiation Treatment for Carcinoma of the Larynx, with Special Reference to the Coutard Method. Trans. 41st Annual Meeting American Laryngological, Rhinological and Otological Society, Inc., pp. 519-522, 1935.
16. Looper, Edward A.: Laryngectomy for Cancer of the Larynx. Surg., Gyn. & Obst., **64**:524-531, 1937.
17. Edling, Lars: Primary Results of Teleradium Treatment in Cancer of the Larynx and Hypopharynx. Radiol., **25**:267-273, 1935-36.
18. Coutard, Henri: The Conception of Periodicity as a Possible Directing Factor in the Roentgentherapy of Cancer. Proc. Inst. Med., Chicago, pp. 310-323 (Oct. 15) 1935.
19. Coutard, Henri: Cancer of the Larynx: Results of Roentgen Therapy after Five and Ten Years of Control. Amer. Jour. Roentgenol. & Rad. Ther., **40**:509-516 (Oct.) 1938.
20. Thomson, Sir St. Clair: Cancer of the Larynx.

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DISCUSSION (*Abstract*)

Dr. John H. Foster, Houston, Tex.—Some men can see no good in anything but surgery except in extensive extrinsic cases. Up until very recent times there was much to substantiate such a view. Sir Sinclair Thomson established the great value of laryngofissure in cordal cancer and we in America have found it an easy operation with no mortality and splendid results in properly selected cases. MacKenty, Lynch and others developed the technic of laryngectomy until it became a comparatively simple procedure with an almost negligible mortality and a high percentage of cures in more advanced intrinsic cases.

On the other hand, some men do not feel capable of doing the necessary surgery, or are radiation enthusiasts, and refer all cases for radiotherapy. The advent of the radium bomb and the development of fractionated high voltage x-ray therapy have given a powerful impetus to radiotherapy. Enthusiasts for this line of treatment seem to forget two important points upon which Dr. Arbuckle quotes Coutard, namely: (1) Some

types of cancer are very radiosensitive and some are resistant; (2) in order to get the best results with radiotherapy the tumor and the tissue surrounding it must be under constant observation to regulate the dosage. Most of us must turn this treatment over to a radiologist who gives his interpretation, or modification, of the Coutard technic. He cannot observe the larynx and if we examine the case from time to time we do not know enough about the therapy to advise intelligently. Some time ago I was congratulating Dr. Hays Martin at the General Memorial Hospital on some excellent results. He attributed much of it to the fact that he had entire charge of the case. If he felt that surgery was indicated, he operated; if he thought radiotherapy was indicated, he advised that and prescribed the dosage throughout the treatment. Harmer has gotten good results by placing radium needles against the tumor after a window resection of the thyroid ala. I do not believe this method will ever be generally adopted.

If we are to take the responsibility of treating cancer of the larynx, we should study each case individually, weigh the advantages of each type of treatment under the immediate circumstances and advise accordingly. While the advance of knowledge necessitates an adjustment of our sights from time to time, in the meantime we should have some very definite convictions on the subject. If in stating mine I appear dogmatic, may I say that I am giving simply my opinion, which I may have occasion to change later.

In an ordinary case of cancer of grade one or two, I think a laryngofissure gives the best chance of a good result and that the treatment is less severe than radiation. In cordal cancer of the more undifferentiated types I sometimes remove the tumor as thoroughly as possible under direct laryngoscopy and then use fractionated x-ray therapy. We have had a few cases that on laryngofissure were found to be more extensive than expected, cases where a laryngectomy was really indicated. We removed the growth as thoroughly as possible, used the desiccating current on the surrounding tissue and gave x-ray treatment with excellent results to date.

In extensive intrinsic carcinoma we are faced with a decision between laryngectomy and radiation. Here again the type of tumor must be considered. My preference is for laryngectomy in cases of grades one and two and radiation for those of a higher degree of malignancy. With all due respect to Dr. Hays Martin, I cannot agree with his opinion that all cases not suitable for laryngofissure should be treated by radiation. Too much stress is given the seriousness of a laryngectomy and the pitiable plight of a patient deprived of his larynx. I have never had an operative death from the operation or a patient that was not happy afterwards except where there was a recurrence. The operation has been considerably simplified recently by the removal of the larynx sub-perichondrially as described by Crowe.

Extrinsic carcinoma is generally considered inoperable and referred to the radiologist, despite the fact that many of these cases have been saved by surgery. At the last meeting of the Triological Society, Fletcher Woodward brought out an important point in regard to these cases. He said that where the case has become extrinsic the cartilages are affected; if it is given intense radiation there is a breaking down of the cartilage and the case dies of pneumonia or lung abscess. If the larynx is removed and then x-ray therapy given the case will probably recover. This view was substantiated by the guest radiologists.

In conclusion, I am impressed with the efficiency of surgery followed by radiation in many cases. It seems to me that we get quicker and better results if the growth is removed and then radiation applied than if we depend upon radiation alone. This seems rational to me.

Dr. Wendell G. Scott, St. Louis, Mo.—We have been associated closely with Dr. Arbuckle in his work on the treatment of laryngeal cancer, and he has made an earnest effort to arrive at a just evaluation of the effectiveness of the roentgen treatment of this disease. This association has been very profitable because it has been one of mutual cooperation.

The views expressed by Dr. Arbuckle are those that are held by the more progressive laryngeal surgeons who have had an opportunity to observe and work with radiologists who are doing a careful, fractionated roentgen treatment for cancer of the larynx. Chevalier Jackson, in a recent publication, states that he is turning more and more patients with laryngeal cancer who are in an operable stage over to a competent radiologist for treatment. At the present time it is our belief that the trend is undoubtedly in favor of roentgen therapy in cases on which, heretofore, a total laryngectomy would have been performed. However, we are not willing to do away with total laryngectomy absolutely, for there are some cases where the mechanical obstructions are such that this operation can be of value.

Dr. Murdock Equen, Atlanta, Ga.—Prior to the brilliant work of Coutard, x-ray was considered only an adjunct to surgery, but today there are those who go so far as to say that the x-ray should supplant surgery. As with anything new, it is always accompanied by a wave of enthusiasm, and it is well to consider its dangers as well as its virtues. Dr. Jackson has called attention to the danger of the ray and reports a case in which the entire larynx sloughed away. When a laryngeal tumor presents itself, the surgeon must decide which operation he thinks will be best for that particular patient. The various methods to be considered are the removal of the tumor from above by using the Lynch suspension, the method of Jackson, a laryngofissure, a total laryngectomy if the growth has progressed so far that only that will save the life of the patient, or to cast all these methods aside and depend entirely on the x-ray.

It is well to remember that following the administration of therapy and its subsequent failure, surgery cannot follow. This is due to the matting together of the tissues, which is followed by excessive bleeding at the time surgery is attempted or postoperatively and a marked slowing or failure of the wound to heal. Marshall Taylor has called attention to the value of an x-ray study of the larynx with particular attention to various factors which influence the ossification of the cartilages, and he made a plea for its more frequent use. He found that malignancy seemed to hasten the process of ossification in tumors in those cases where the process was slow-growing and had not already caused the destruction of the cartilages.

Dr. Sidney Israel, Houston, Tex.—Wherever surgery is indicated, it still should hold preference over any other form of therapy when dealing with cancer. The most

important decision is to determine the proper indication for any therapy other than surgery. Surgery, when indicated, has given by far the most brilliant results with the minimum of recurrences.

Radiation therapy has made great strides through improvement of technic, recognition of its limitations, and the proper application, both as to dosage and the part affected. Brilliant results have been accomplished by means of therapeutic radiation in many cases generally assumed to be inoperable. Surgery, however, offers the greatest number of permanent cures.

The type of operation and treatment of cancer of the larynx is controlled by the duration and location.

One's surgical consideration of cancer of the larynx should not be different from one's attitude towards cancer elsewhere in the body. Surgery occupies the foremost place in our therapeutic measures and radiation therapy is next.

THE HYPERTENSIVE FACTOR IN WILMS' TUMOR*

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In this paper blood pressure observations are reported in 18 cases of Wilms' tumor with the effects of x-ray therapy, nephrectomy, recurrences, and metastases. The ages of these patients ranged from 8 months to 9 years with an average age of 4 years and 2 months. For children in this age group we considered a systolic blood pressure below 110 mm. mercury as normal, 110 to 125 mm. as moderately elevated, and above 125 mm. as extremely elevated. Using these criteria, there were 4 cases with normal blood pressure, 6 with moderate elevation, and 8 with extreme elevation. All of these children had palpable masses in the flanks, but there was no definite relationship between the size of the mass and the height of the blood pressure. Day,[1] in his recent article, says that blood pressure determinations for small infants are at best unreliable. Most of the children in this group had daily blood pressure recordings and the figures reported here represent mean readings rather than isolated determinations. Day also showed that the systolic blood pressure readings vary inversely with the width of the cuff. Our determinations were made with a mercury manometer and a 10 cm. cuff which we believe afforded comparatively accurate blood pressure estimations.

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Effect of X-Ray Therapy on Hypertension.—Three patients with extreme hypertension had marked reductions in blood pressure within 3 weeks following x-ray therapy (164/130 to 110/70, 140/95 to 105/65, and 160/80 to 115/80). However, in the first case there was hemorrhage into the tumor (proved after neprectomy) with resulting shock and anemia. The blood pressure did not rise above the normal level in spite of the fact that the shock and the anemia were successfully combated by appropriate measures. In another case, extreme hypertension was not influenced by x-ray therapy. In 6 patients having normal or moderately elevated blood pressures no appreciable change was noted following x-ray therapy. One of these patients with normal blood pressure received 2,500 R. U. of x-ray and 4 weeks later underwent nephrectomy. She returned in 2 months with signs of acute glomerulonephritis and the blood pressure was 150/120. Twelve months later the blood pressure was still 150/120. No recurrences of metastases could be demonstrated. Although x-ray nephritis has been produced experimentally in dogs[2] and rabbits[3] by irradiation of the kidneys, the possibility in this case seems remote because of the relatively small dosage. This view is even more plausible since another patient of about the same age received 5,000 R. U. of x-ray over a five-months period without showing any signs of nephritis or elevation in the blood pressure. Irradiation in all of these cases brought about the usual dramatic shrinkage of the tumor.

Effect of Nephrectomy on Hypertension.—The blood pressure of three patients having extreme hypertension reduced following x-ray therapy remained at normal levels after nephrectomy. Another patient with extreme hypertension which was unaffected by x-ray therapy still had extreme hypertension four weeks after nephrectomy. According to the experimental work of Wilson and Byron,[4] such a failure is to be expected if the hypertension had existed long enough to produce sclerotic changes in the vessels of the other kidney before the diseased kidney was removed.

Effect of Recurrences on Hypertension.—One patient with extreme hypertension which was reduced following x-ray therapy and nephrectomy had normal blood pressure 5 months later in spite of local recurrence of the tumor. Twelve months later, when this patient was dying of local recurrence and metastatic tumor, the blood pressure was moderately elevated. Another

patient dying of metastasis to lungs 17 months after nephrectomy had normal blood pressure.

Effect of the Tumor Type on Hypertension.— Wilms' tumors are essentially "mixed" as regards cell types. Some have a predominance of epithelioid cells, and some of mesoblastic cells, while still others have the different cell types in about equal proportions. In this series the predominant cell type had no influence upon the presence or absence of hypertension.

DISCUSSION

From clinical and experimental data* it seems that unilateral renal ischemia is capable of causing a sustained rise in arterial pressure which, if allowed to continue, produces sclerotic changes in the arterioles throughout the general circulation, including that of the other kidney. These changes *per se* are capable of both producing and maintaining hypertension. Under such conditions the removal of the primary ischemic kidney would not be followed by a return of the blood pressure to normal levels. The association of hypertension with certain types of chronic renal disease has been recognized since Bright first made the observation over a hundred years ago. It is also known to occur frequently with polycystic kidney disease and chronic pyelonephritis. In 1938, Bradley and Pincoffs[5] observed hypertension in 5 consecutive cases of Wilms' tumor. In two of their cases the blood pressure came down after nephrectomy only to rise again with local recurrence. They did not think that it was due to mechanical interference with the renal blood supply, but that the tumor tissue in these neoplasms had the "property possessed by renal tissue of causing an elevation in arterial pressure when it is altered by certain types of damage." However, they were unable to demonstrate the presence of a pressor substance in the tumor tissue.

It seems most likely that the hypertension frequently but not always associated with Wilms' tumor is the result of renal ischemia produced mechanically by the tumor. If it were due to a pressor substance elaborated by the tumor tissue, it should be present in every case and should return with all recurrences and metastases. This is obviously not in accord with the facts observed in the cases reported herein. The hypertension associated with local recurrence observed in two cases reported by Bradley and Pincoffs[5] and in one case in this series is best explained on the basis of renal ischemia resulting from tumor growth about the pedicle of the remaining kidney. In our case the hypertension did not reappear until the local recurrence had become quite extensive.

Irradiation probably reduces the hypertension by reducing the size of the tumor mass and thereby lessening the amount of ischemia. Irradiation of the adrenal glands has caused reduction of the blood pressure in cases of essential hypertension,[13] and this factor must also be considered in these cases. On the other hand, hypertension has been produced in experimental animals (dogs) with x-ray irradiation,[2] and it is entirely possible that a large quantity of x-ray therapy will cause a subsequent elevation in blood pressure due to renal ischemia from the resulting obliterative endarteritis. This does not seem probable in the dosage generally used. However, if the hypertension has been maintained sufficiently long to have produced sclerotic changes in the arterioles of the other kidney, neither irradiation nor nephrectomy will bring about a return of the blood pressure to normal levels.

It is interesting to note that in this series the only patients living as long as 12 months without evidence of local recurrence or metastasis had normal blood pressures when first seen. Hypertension associated with Wilms' tumor is probably indicative of tumor growth in the region of the large vessels and for that reason may be of prognostic significance.

CONCLUSIONS

(1) Hypertension is frequently but not always associated with Wilms' tumor. In this series of 18 patients only 4 had normal blood pressures.

(2) It is best explained on the renal ischemia basis.

(3) Irradiation probably reduces the hyper-

*Goldblatt[6] produced a sustained rise in the blood pressures of dogs by constricting the renal arteries. He was of the opinion that the hypertension was due to an "effective substance" or "humoral" elaborated by the ischemic kidneys working in conjunction with the hormone from the adrenal cortex. Glenn, Child and Heuer[7] and Blalock and Levy[8] produced hypertension from induced renal ischemia. Wilson and Byron[4] observed hypertension in rats from the constriction of one renal artery. Changes of nephrosclerosis were produced in the good kidney, but not in the operated kidney. They concluded that the lesions were the result of the hypertension which caused compensatory hypertrophy of the vessel walls. The operated kidney, being protected by the clamp, was spared. Leadbetter and Burkhead[9] and others[10 11] report cases of hypertension associated with unilateral kidney disease thought capable of producing renal ischemia. All were cured of the hypertension by nephrectomy. Lieter[12] reported 3 cases of hypertension explained on the renal ischemia basis.

tension by lessening the amount of renal ischemia.

(4) If the hypertension has existed long enough to have produced sclerotic changes in the arterioles of the good kidney, neither irradiation nor nephrectomy will be followed by a return of the blood pressure to normal levels.

(5) The presence of hypertension associated with Wilms' tumor may be of prognostic significance.

REFERENCES

1. Day: Jour. Ped., **14**:148-155, 1939.
2. Hartman, Ballenger and Daub: Amer. Jour. Med. Sci., **172**: 487-500, 1926.
3. O'Hare, Altnow: Christian; Calhoun; and Sosman: Boston Med. & Surg. Jour., **194**:43-45, 1926.
4. Wilson and Byron: Lancet, **1**:136-139, 1939.
5. Bradley and Pincoff: Ann. Int. Med., **2**:1613-1628, 1938.
6. Goldblatt: Ann. Int. Med., **2**:63-103, 1937.
7. Glenn, Child and Heuer: Ann. Surg., **107**:618-620, 1938.
8. Blalock and Levy: Ann. Surg., **106**:826-847, 1937.
9. Leadbetter and Burkhead: Jour. Urol., **39**:611-626, 1938.
10. Boyd and Lewis: Jour. Urol., **39**:627-635. 1938.
11. Barker and Walters: Proc. Staff Mayo Clinic, **13**:118-121, 1938.
12. Lieter: J.A.M.A., **111**:507-510, 1938.
13. Boswell: Sou. Med. Jour., **31**:1001-1003, 1938.

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WILMS' TUMORS: EMBRYONAL ADENOSARCOMAS OF THE KIDNEY*

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INTRODUCTION

Renal neoplasms are by far the most frequent of urogenital tract tumors which occur in the very young, in infants and children, and because of this the possibility of their existence should be considered more frequently before the condition has progressed to such an extent that therapy is of no avail. In the author's private practice, four cases were observed within a period of three months, but none has been seen since.

History.—In 1828, Gairdner[1] presented the first case of renal sarcoma in an infant. Subsequently in the publications of Eberth[2] in 1872; Conheim[3] in 1875; Sturm[4] in 1875; Weigert[5] in 1876; Osler[6] in 1879; Huber Bastroem[7] in 1879; Brosin[8] in 1884; Doederlein[9] in 1894; Birsch-Hirschfeld[10] in 1894; and Wilms[11] in 1899; the clinical picture and pathogenesis have been established.

Origin.—It is agreed by all that this tumor arises from primitive germinal tissue. Some investigators believe it may come from the Wolffian body, abberrant cells, nephrotome, or endothelium (Conheim,[3] Wilms,[11] Muns,[12] Paul,[13] Eberth,[2] Busse,[14 15] Ewing,[16] Rebbert,[17] Brock,[18] Birsch-Hirschfeld,[10] and others). All of these may be more or less correct, because as Pack and Dean[19] note, the tumor may arise at different stages of the development of the embryonal tissue.

Incidence.—This is the commonest tumor of the abdomen and urogenital tract in childhood; in adults such tumors are very rare. Approximately 50 per cent of all neoplasms in children originate in the eye, but the kidney is second with approximately 20 per cent of all tumors of childhood, as shown by Dean and Pack[19] and others. In the State of Mississippi, in the past in only 13 cases has a diagnosis of Wilms' tumor appeared in the hospital records of 92 hospitals. Undoubtedly many more cases have occurred, but since a large part of our State is in close proximity to two large medical centers, New Orleans and Memphis, many patients have probably migrated to these cities.

Sex.—The published reports indicate an equal distribution of these tumors in males and females, but this was not true of the Mississippi State series. The author's cases were all males, 3 colored and 1 white (Cases 1, 2, 3 and 4 in *Table 1*).

Age.—It is agreed by Campbell,[20] Pack,[19] Dean,[21] Fraser,[22] and others that 75 to 95 per cent of cases appear before the seventh year. This tumor is found occasionally in adults, and in animals (Feldman[23]) such as sheep, swine, rabbits and chickens.

Pathology.—Fortunately the majority of cases of this tumor are unilateral, and only when they are unilateral are we able even to hope for a cure. All of the author's cases were unilateral.

The tumors are situated retroperitoneally and vary in size, depending upon the length of time elapsing from their onset until the growth is stopped by x-ray or surgery. The tumor mass may be smooth (as it usually is early) or lobulated. On first inspection it may resemble an enormous kidney and be separated by a capsule from the kidney itself. Only a few cases have been reported outside the kidney substance. Often the tumor replaces the kidney substance by its overgrowth. Of the author's cases two were in the right kidney and two in the left.

*Read in Section on Surgery, Southern Medical Association, Thirty-Second Annual Meeting, Oklahoma City, Oklahoma, November 15-18, 1938.

Table 1

CASES OF WILMS' TUMORS FOUND IN MISSISSIPPI HOSPITAL RECORDS, INCLUDING AUTHOR'S CASES, NOS. 1, 2, 3 AND 4

No.	Age	Sex	Color	X-Ray Treatment	Surgery	Condition
1	5	M.	C.	Pre-op.	No	Dead
2	3	M.	C.	Post-op.	Yes	Dead
3	3	M.	C.	Yes	No	Dead
4	1	M.	W.	Pre-op.	Yes—18 mos.	Living and well
5	1	M.	W.	No	Yes	Dead
6	4	F.	W.	Pre- and post-op.	Yes	Dead
7	2	M.	W.	Post-op.	Yes—5 years	Living and well
8	5	M.	C.	Pre- and post-op.	Yes	Dead
9	5	M.	C.	None	None	Dead
10	2	M.	W.	None	Yes	Dead
11	3	M.	C.	None	Yes	Dead
12	1½	M.	W.	None	Yes	Dead
13	4	M.	C.	None	Yes	Dead
Total 13	1-5	Males 12-1		X-ray pre-op. — 4 X-ray post-op. — 3 Combined—2		

1 case living and well 18 mos. Pre-op. x-ray only and surgery.
1 case living and well 5 years. Post-op. x-ray only and surgery.
Deaths 11, living 2.
Operation 10 cases, inoperable 3.

It is generally agreed that Wilms' tumors are composed of tissue of mesodermal origin. Striated muscle, myxomatous tissue, fat, cartilage and cells from the renal blastoma make up this mixed tumor which apparently has a mesodermal origin at some time during the development of the anlagen.

Symptoms.—As Kretschmer[24] has said,

"As a rule, the symptoms of this group of tumors are general, rather than urological, and the urological symptoms, even when present, occupy a relatively unimportant position."

The principal symptom in most cases is progressive tumefaction, generally smooth, in the abdomen of a young child. Attention is directed to the tumor by: (a) increase in size of abdomen as indicated by tightness of clothing; (b) a fall causes an examination to be made and tumor noted; (c) "pot belly" observed by parents who request examination for intestinal parasites; and (d) rarely by pain.

Malaise, constipation, urinary findings, pathologic anemia, loss of weight, fever, edema, and shortness of breath are all symptoms that occur late in the progress of the case.

Diagnosis.—The diagnosis should usually offer no difficulty. As a former teacher, W. D. Haggard,[25] with whom I was associated as a student, has said:

"Surgery is the Queen of Arts and the inherent ability and result of careful teaching with competent training gives the surgeon the ability to sum up such findings as he has at hand in these cases of Wilms' tumors which he has obtained from his two God-given senses, sight and touch, and almost always gives him the ability to make a diagnosis of a retroperitoneal tumor in these children and then, if necessary, prove it right or wrong by further exhaustive study."

Lake and Ayers[26] note that tests for diagnosis of the tumor are of little value.

Plain x-ray examination may show a tumor displacing the intestines downward and medially. Barium in the colon may demonstrate this better and more easily. Intravenous pyelograms and retrograde pyelograms may show a deformed kidney pelvis, and usually little if any dye is excreted on the diseased side. Kidney function test on the good kidney is necessary before operation. Intravenous pyelograms usually will serve as a function test when the technic is carried out correctly.

It is never necessary to perform biopsy, which encourages spread through the capsule of this malignant growth and may be followed by its rapid extension, regardless of the method of biopsy used (Campbell, M. F.[20]).

PROGNOSIS

The outcome is fatal in the majority of cases, but I believe that if we outline a definite plan of treatment to the family and secure proper cooperation from them, we shall gain more cures in the years to come.

Of the 13 cases of Wilms' tumors reviewed in Mississippi and heretofore unreported, the deaths were 11, with 10 operative cases and 3 inoperable. Four of these cases received preoperative x-ray, three postoperative x-ray, and two both pre- and postoperative x-ray. Four of these cases are reported in detail in this paper. Total mortality for the series of 13 cases is 84.62 per cent (11 dead) with 2 living, or 15.38 per cent. Mortality of the author's series is 75 per cent (*Table 2*).

TREATMENT

This consists of preoperative irradiation, surgery and postoperative irradiation with supportive treatment. It is my opinion that no case requiring postoperative irradiation has been cured and that its use is only palliative. When preoperative irradiation shrinks a tumor within its capsule, which it has not outgrown, and that tumor is removed *in toto*, postoperative irradiation is not actually necessary; but when the tumor has extended beyond the confines of its capsule all known and combined forms of therapy are necessary. These tumors are unusually radiosensitive and can be melted in a short time by x-ray only, but it is almost inevitable that they will return and it is during this period of recession that surgical removal of this tumor is carried out at the ideal time.

Table 2

SHOWING DEATHS FROM "CANCER OF KIDNEY" AS COMPILED BY MISSISSIPPI STATE BOARD OF HEALTH; NEED FOR MORE COMPLETE CAUSE OF DEATH CLASSIFICATION IN THIS TYPE OF DISEASE. ELEVEN OF THE THIRTEEN CASES SEEN ARE SHOWN IN THIS SERIES OF DEATHS*

	Male		Female	
1937	White	Col.	White	Col.
Under 1 year	0	0	0	0
1 year	0	0	1	0
2 years	1	0	0	0
3 years	1	1	0	0
4 years	0	1	0	0
6 years	0	0	1	0
6-10 years	0	0	0	0
Total	2	2	2	0
1936				
Under 1 year	0	1	0	0
1 year	0	0	1	0
Total	0	1	1	0
1935				
2 years	1	0	0	0
6 years	0	1	0	0
8 years	0	0	1	0
Total	1	1	1	0
Total 11	3	4	4	0

*International list of causes of death makes no special subdivision of cancer of kidney or Wilms' tumors.

Dean reports that he has two cases living with x-ray therapy only, but it stands to reason and common sense that it is almost imperative to remove this mass after it has had sufficient x-ray treatment to eliminate the possibility of its recurrence.

In order to prevent movement during deep x-ray therapy, the patients are sedated by the administration of 0.2 c. c. per pound of body weight of paraldehyde administered either by stomach catheter or by rectum in starch solution. They are also fixed to a cross-like frame (*Fig. 1*). Three portals of irradiation, anterior,

Fig. 1

Cross to which patients are fastened after paraldehyde has been administered to assure us of no movement in x-ray treatment or operation.

lateral and posterior, are usually used, but more may be necessary if the tumor is large. Liver, pancreas and other organs are protected by lead. In two to three weeks following the therapy the tumor is usually shrunken to its minimum size, which is the ideal time for surgical removal.

The anterior transperitoneal approach is the ideal one for the removal of the tumor, because it permits the removal with less perirenal manipulation than in the lumbar approach.

Supportive therapy (whole blood, fluids and general palliative treatment) is carried out with the average length of stay in the hospital of eight days. Treatment, as a whole, in the past (as carried out generally) has been unsatisfactory. Important points are: early treatment; intensive preoperative x-ray treatment; and surgical removal by anterior approach. Case 4 of this series exemplifies the ideal form of therapy as well as excellent cooperation on the part of the family.

CASE REPORTS

Case 1.—L. W., aged 5, was admitted to the hospital April 17, 1937, his chief complaint a swollen abdomen.

The child was taken to the family physician because its abdomen was getting larger and purgatives and worm medicine purchased at the drug store did not reduce it.

He had had measles, mumps, pertussis and a fractured left forearm in 1936.

On entrance his temperature was 101°, pulse 104, and respiratory rate 26.

Examination was negative except that a large mass was noted in the right abdomen, which was smooth and reached within one finger breadth of the umbilicus and to about three finger breadths of the wing of the ilium and disappeared beneath the costal margin.

Laboratory examination showed: white blood cells 19,000 with 82 per cent polynuclears, 10 per cent small lymphocytes and 8 per cent large lymphocytes. Hemoglobin was 80 per cent, red blood count 4,900,000, and the urine was negative chemically and microscopically. An intravenous pyelogram showed a good outline of the left kidney pelvis and ureter with very little concentration of the dye in the right kidney pelvis in one area, but no outline of the pelvis or ureter could be seen, but a soft pale shadow could be outlined over this area.

The diagnosis was Wilms' tumor. On April 20, 1937, x-ray therapy was started and 300 r were given anteriorly, laterally, and posteriorly on each of three days and the patient discharged on April 22, 1937, with instructions to return in three weeks. The patient did not return nor respond to written requests, but did return on July 6, 1937, at which time the tumor was as large as before. The family said that it had gone down a great deal, but when it began to come back they returned for treatment. X-ray was repeated as previously with instructions to return in two weeks. The patient did not return for treatment and died on September 11, 1937.

Case 2.—C. V. (No. 564), aged 3, was admitted to the hospital March 1, 1937, the chief complaint, swollen stomach.

The stomach had been getting larger for the previous four months, but had grown more rapidly in the preceding month. He had been fretful and had lost a great deal of weight. He had had no trouble with his urination. His appetite had been good until the previous few days, when fever set in. Since then he had been fretful with nausea and vomiting and the swelling of his abdomen had increased.

His temperature was 99°, pulse 96, and respiratory rate 22.

He was an emaciated child with a large abdomen and very little flesh on the chest, with prominent ribs. There was marked distention of the abdomen with several large stony masses in the left abdomen. The mass could be felt by rectum and seemed to be lobulated. It extended into the flank and disappeared beneath the costal margin.

Laboratory examinations showed the urine negative, red blood cells 695,000, white cells 5,250, hemoglobin 25 per cent, differential count, polynuclears 38 per cent, small lymphocytes 34, and large lymphocytes 28.

It was felt that this child had a Wilms' tumor which had invaded surrounding structures and it was deemed advisable to give extensive x-ray therapy and have him return. An intravenous pyelogram was done; no dye was excreted on the left and a very poor shadow of the kidney pelvis was obtained on the right side, but a soft tissue mass was outlined on the left. He was given two transfusions of 225 c. c. of citrated blood and was sent home to return in three weeks.

The patient did not return for further treatment and died on July 16, 1937.

Case 3.—W. D. F. (No. 1360), aged 3, was admitted April 22, 1937, his chief complaint, pain in the left side with nausea and vomiting.

The onset of his illness occurred April 21, 1937, when the child was playing in the yard. He fell on a two-gallon stone jug, sticking its neck into his left side. This was followed by nausea and vomiting and fever of 101-102°. He had vomited the day of examination with much pain in the left side on vomiting. He would take no food, but drank water. He had had no bowel movement since injury, but urination had been normal.

Physical examination showed a temperature of 101 4/5°, pulse 140, and respirations 28. The left abdomen was rigid with bulging of the left flank and a palpable mass in the left upper quadrant. There was muscle defense over the whole abdomen. Rectal examination revealed nothing.

Urine examination was negative. The red blood count was 2,045,000 with 60 per cent hemoglobin. The white count was 12,200, differential, 82 per cent polynuclears, 7 per cent small lymphocytes and large lymphocytes 12.

It was our impression that this child probably had a large spleen (malaria?) which it had ruptured on falling on the jug neck.

Operation was done the day of admission and a black retroperitoneal mass was seen with a normal spleen. This was opened and much blood with granular tapioca-like material was encountered. Further exploration showed a ruptured Wilms' tumor of the left kidney as proven by the pathologist and the whole mass with left

Fig. 2
Ruptured Wilms' tumor and kidney as removed from *Case 3*, which had been diagnosed ruptured spleen.

kidney was removed and the area drained (*Fig. 2*). A transfusion was given on the table from the father and the recovery was uneventful. On May 4, 5 and 6, 300 r of aluminum and copper filtered deep x-ray therapy from a 200 kilovolt machine were given over the anterior lateral and posterior portals, respectively, and the patient was discharged on May 9, 1937.

The patient was readmitted May 24, and on May 24, 25 and 26 this treatment was repeated and at this time he seemed to be doing well.

The patient was readmitted June 20, 1937, with a large palpable mass in the left upper abdomen, a red blood count of 2,200,000, 50 per cent hemoglobin, and a negative urine. He was given 250 c. c. of citrated blood and the above deep therapy repeated on three successive days. The patient's father was instructed to return with him in three weeks, but nothing further was heard from this patient until his death on October 21, 1937.

Case 4.—J. H. (No. 771), a white boy of 11 months, was admitted February 16, 1937. The chief complaint was of a swollen abdomen.

This patient had been seen by me on my plantation in Yazoo County when the father and mother became worried because of the enlargement of his abdomen and they thought his arms and legs were getting smaller. He had no pain and no trouble of any kind, but he seemed to be getting pale and not gaining in strength and weight.

He appeared to be barrel-shaped in the torso with his legs and arms thin and smaller in proportion. There was a mass in his right side which extended to the umbilicus in the midline and to the crest of the ilium below. It was hard, smooth and firmly fixed. The border of the liver could be delineated as it disappeared beneath the costal margin. There was a tympanitic note to the abdomen over it and x-ray with barium showed the colon in front, but displaced downward slightly (*Fig. 3*).

The urine was negative. The red blood count was 3,260,000, hemoglobin 60 per cent, white count 12,260, and differential 72 per cent polynuclears and 28 per cent lymphocytes.

An intravenous pyelogram showed a small speck of dye on the right in a shadow caused by increasing soft parts density; the left side was normal.

The diagnosis was Wilms' tumor.

Dr. Horton Casparis and Dr. Barney Brooks, of Vanderbilt University, saw this child and agreed that there was a retroperitoneal tumor, but Dr. Brooks was inclined to consider it an adrenal tumor or a neuroblastoma.

On February 16 and 17 deep therapy was given over two portals under paraldehyde anesthesia. On March 16, 1937, the tumor had almost disappeared beneath the costal margin and was removed by the anterior approach (*Fig. 4*). A transfusion was given on the table. An uneventful recovery was made. This child had been observed each month for the past year and a half and has had no further x-ray treatment. It can easily be seen from the tumor that it was entirely encapsulated and was removed *in toto* with no possibility of extension and therefore no necessity of further treatment (*Fig. 5*).

SUMMARY

A brief review is given of the rather voluminous literature of this subject, with presentation of the common salient points and a rather full bibliography for your reference with the addition of 4 cases to the literature, with 13 cases total found in Mississippi.

Emphasis is hereby placed on the rather simple method of diagnosis by sight and touch, bearing in mind the possibility of such a tumor. The diagnosis is confirmed by plain x-ray plates and

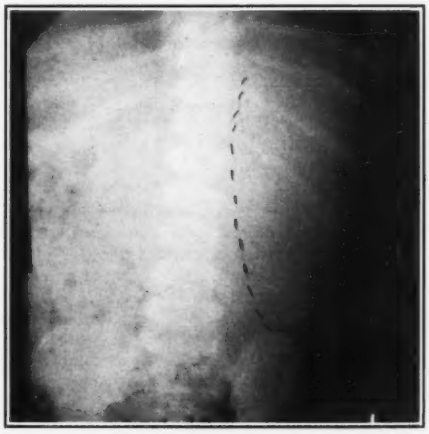

Fig. 3
Flat plate of *Case 4* showing outline of soft parts mass in right abdomen (retroperitoneal).

intravenous (and retrograde when necessary) pyelograms.

X-ray therapy should be used in every case, preoperatively to the point of shrinking the tumor mass. The growth should then be removed *in toto* without breakage and without destroying its natural barriers. The transperitoneal approach for its removal is preferable.

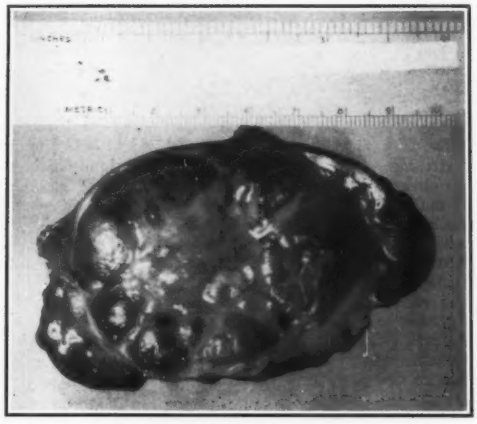

Fig. 4
Tumor from *Case 4* showing complete encapsulation with very little kidney remaining.

Fig. 5
Case 4, showing condition on October 10, 1938, twenty months postoperative, age thirty-one months. No evidence of recurrence, therefore cured.

Biopsy by any method is condemned since it breaks open the capsule which is the natural barrier.

There is an optimal time for removal of this tumor and it falls in the period after the shrinking of the tumor mass before its regrowth starts.

The necessity is shown in Cases 1 and 2 of outlining the treatment to the parents, explaining the various forms of therapy used and gaining their cooperation by taking them into one's confidence.

A simple method for assuring the immobility of the patient while giving the necessary x-ray therapy is presented herein.

A series of 4 cases is presented with 1 case cured because of its type, location, ideal form of therapy and explicit cooperation on the part of the family, emphasizing again the necessity for cooperation.

Recurrence of the tumor indicates failure of treatment, after which no form of therapy offers any hope, though x-ray is palliative.

I am deeply indebted to Dr. Alton Ochsner for his kind and constructive criticism in the completion of this manuscript.

BIBLIOGRAPHY*

1. Gage, H.; and Adams, D.: Ann. Surg., **78**:229, 1923.
2. Dolerlein: Centralb. F. d. Krankh. d. Harn. U. Sex Org., **1**:—, 1897.
3. Conheim, J.: Virchow's Arch. t. Path. Anat., **65**:64, 1875.
4. Slesinger: Proc. Roy. Soc. Med. (Urol. Sect.), **20**:719, 1927.
5. Trappe: Ztsche f. Path., **1**:130, 1907.
6. Muhl, G.: Nord. Med. Tidskr., **13**:273, 1937.
7. Holloway, L. W.: Jour. Fla. M. A., **10**:229, 1924.
8. Bothe: Amer. Jour. Roentg., **33**:529-536, 1935.
9. Deming, C. L.: J.A.M.A., **80**:902, 1923.
10. Birsch-Hirschfeld, F. V.: Beitr z. Path. Anat. u. z. allg. Path., **24**:343, 1898.
11. Weigert: Virchow's Arch. f. Path. Anat., **67**:492, 1876.
12. Mathews, F. P.: Jour. Amer. Vet. Med. A., **74**:238, 1929.
13. Nicholson, G. W.: Jour. Path. and Bact., **34**:711, 1931.
14. Brock, G.: Virchow's Arch. t. Path. Anat., **140**:493, 1895.
15. Busse, O.: Virchow's Arch. t. Path. Anat., **157**:346, 1899.
16. Eve, F. S.: Tr. Path. Soc., London, **33**:312, 1884.
17. Pincoffs and Bradley: Tr. Amer. Ann. Phys., **52**:320-5, 1937.
18. Brosin: Virchow's Arch. t. Path. Anat., **96**:453, 1884.
19. Clayton: Jour. Tenn. St. Med. Assn., **26**:475-9, 1933.
20. Bugbee, H. G.; and Wollstein, Martha: J.A.M.A., **83**:1887-94, 1924.
21. Dean, A. L., Jr.; and Pack, G. T.: J.A.M.A., **98**:10-17, 1932.
22. Freitag: Beitr z. Path. Anat. u. z. allg. Path., **24**:393, 1896.
23. Ewing: Neoplastic Dis., 3rd ed., p. 796. Philadelphia: W. B. Saunders Co., 1928.
24. Keyes, E. L.: Jour. Urol., **39**:3, 384, 1938.
25. Garceau: Renal, Ureteral, Peritoneal and Adrenal Tumors, 1906.
26. Kretschmer, H. L.; and Hibbs, W. G.: Surg., Gyn. & Obst., **52**:1-24, 1931.

*The manuscript originally had one hundred and fifty-two references. Only those specifically mentioned in the text are here given, twenty-six in all.

DISCUSSION (*Abstract*)

Dr. Basil A. Hays, Oklahoma City, Okla.—During the past three years we have seen six cases of Wilms' tumor in University Hospital, and I append a table (bottom of page) detailing the salient points of each.

You will note that the one constant finding was a tumor in the abdomen, whose average duration was about three months before the patient came to the hospital. Blood was found in the urine of only two cases and in those it was microscopic in amount. Pain was not a symptom; fever occurred in only three cases, while gastro-intestinal symptoms were prominent in three. One was subjected to nephrectomy and made a good recovery, but returned to the hospital and died after a lapse of 72 days, showing heavy metastatic processes in the lungs. The others were all too far advanced or the parents were unwilling to have them operated upon. I am glad to learn that Dr. Long has found preoperative irradiation of considerable value. Postoperative irradiation, however, in my experience is utterly worthless and only causes distressing reactions.

In a recent article Rodelius has called attention to some remarkable differences between tumors of the kidney occurring in adults and in children. He points out that the most frequent kidney tumor seen in adults is hypernephroma, while in children it is Wilms' mesodermal tumor. In adults, kidney tumors comprise 0.5 per cent of all tumors, whereas in children it is 20.4 per cent. It is further noteworthy that in adults the organ is practically entirely destroyed by the invasive process, whereas in children the kidney grows right along with the tumor and is apparently able to maintain its structure for quite a period of time. Also the prognosis in the two groups is quite different. A considerable number of adults who have had kidney tumors removed have survived, approximately 30 per cent. On the other hand, the permanent cures in children have never been reported as greater than 10 per cent. In adults the classic triad of symptoms is palpable tumor, hematuria, and pain. Of these pain occurs relatively rarely in children, hematuria likewise, and palpable tumor is the only real symptom that can be depended upon. On the other hand, in children gastro-intestinal symptoms are of frequent occurrence. The usual thing that brings a child to the doctor is a swelling in one side of the abdomen, although occasionally the presenting symptom will be anemia, malaise, fever, or gastro-intestinal symptoms. When the swelling is first noticed, an intravenous pyelogram will give all the information needed to clinch the diagnosis and to reveal the functional efficiency of the opposite kidney so that operation can be carried out as early as possible. As the disease progresses other symptoms and signs may occur such as varicocele, edema, widening of the abdominal veins or swelling of the scrotum on the affected side. The important thing every physician should remember is that with the single exception of enlargement of the spleen in lues or malaria, any tumor of the abdomen occurring in a child is most likely to be a Wilms' adenosarcoma of the kidney because practically no other growth occurs in this region at this age.

Dr. Russell A. Hennessey, Memphis, Tenn.—The essayist has chosen for his theme a condition which we are obliged to approach, with our present day knowledge of malignancies, much as we do tumors of the testes or malignant tumors of the lactating breast and many others. Until such time as a better understanding of the development and cause of malignant tumors has been gained, our efforts at best must be admittedly feeble and uncertain. Likewise, a wide divergence of opinion regarding the management or treatment of such lesions is further admission of our shortcomings and provides enviable opportunities for the continued operations of quacks and perpetrators of cancer cures.

Fortunately, indeed, renal tumors in children occur but one-fourth as often as in adults, in whom the incidence of renal neoplasms is cited as one-half of 1 per cent. While embryonal adenosarcoma of the kidney is most commonly found in children, there have been, according to Alcorn, about twenty-five cases reported in adults. Their clinical recognition is, as a rule, not difficult. Most frequently, the first abnormality noted has been a rapidly increasing abdominal mass or enlargement of the abdomen. It has been noted by some observers that the abdominal mass is particularly inclined to protrude forward rather than into the flank and may be regular or irregular, firm or soft, movable or immovable.

Most often, examination of the urine provides little information in the early development of the disease.

JULY, 1935, TO JULY, 1938: 3 YEARS

Age	Sex	Side	Duration	Hematuria	Pain	Tumor	Fever	Gastro-Int.	Nephrectomy	Result
1.11 mos.	M	R	4 mos.	—	—	+	+	—	+	Died 72 days post-op.
2.16 mos.	F	L	3 mos.	—	—	+	—	++	—	Unimproved
3.10 mos.	F	L	1 mo.	—	—	+	—	—	—	Unimproved
4.10 mos.	M	R	1½ mos.	—	—	+	+	—	—	Unimproved
5.3 yrs.	F	L	8 mos.	25 RBC	—	+	+	+	—	Unimproved
6.5 mos.	F	R	1 mo.	4+ alb. Few RBC	—	+	—	+	—	Unimproved
Average 14⅓ mos.	2 M 4 F	R3 L 3	3 mos.	2 micro.- 4 neg.	—	+	3 F 3 0	3 G-I 3 0	Op. 1 Not 5	

Priestly and Broders, in the analysis of 65 cases, however, found hematuria as the presenting symptoms in 28.9 per cent and at some time in the course of the disease in 43.4 per cent. Fever has also been common to the disease, occurring in about 50 per cent of cases and rising at times, as in two cases observed by us, to 104° F. It was a symptom present in all four cases observed by us.

The presence of high blood pressure with tumors of the kidney was observed first by Vollhard. Pincoffs and Bradley have observed this phenomenon in four cases of Wilms' tumors which they have studied, and it was present in one case that has come under our care.

Because of the extremely high degree of malignancy of embryonal adenosarcoma, all forms of treatment have proven most unsatisfactory and, despite all therapeutic efforts, the mortality remains at 95 per cent or more. It is generally agreed, however, that nephrectomy with pre- and postoperative irradiation provides perhaps the best opportunity for cure of the disease. Priestly and Broders found that the group that was treated by irradiation and nephrectomy survived approximately twice as long as the group which was treated either by operation or irradiation alone. Priestly and Broders further state that the effect of irradiation on these tumors is evidenced both histologically and grossly by disintegration and necrosis, or by no change whatever. This involves further discussion of the variable radio sensitivity of renal tumors, but may explain the success with irradiation alone reported by Pohle and Ritchie and W. H. McNeill. In both instances, irradiation was carried out over a period of three to three and one-half years. McNeill emphasizes the necessity of including the chest and abdomen in the irradiated fields.

Dean states that if by radiosensitivity one implies diminution in the size of a renal tumor under the influence of x-ray, many tumors of the kidney should be so classified, but if by this term it is meant that sterilization of tumors of the renal parenchyma can be accomplished by external irradiation, he has found that the majority of such tumors are radioresistant.

William E. Ladd, after a study of forty-five proven cases of Wilms' tumors, reported fourteen living with eleven probable cures, the length of time varying from one and one-half years to nineteen and one-half years. He urges nephrectomy without the delay incident to a course of preoperative irradiation, saying that more cures have occurred following this method of treatment, and he is also of the opinion that preoperative irradiation facilitates the operation and immediate operative mortality only at the sacrifice of an increased late mortality.

Our experience with Wilms' tumors is limited to four proven cases in the past twelve years, each of which, despite approved methods of treatment, consisting of irradiation and nephrectomy, suffered recurrences within six months and fatal terminations. In this group, there were two males and two females of the following ages: three years, 2; three months, 1; and eleven weeks, 1. The duration of symptoms was seven months, six months, one and one-half months and one month, respectively.

In making a surgical approach upon a renal tumor of any considerable size, it has been our experience that a combined lateral rectus and lumbar incision provides a better method of reaching and dealing with the renal pedicle.

It would seem then that until such time as the genesis of malignant tumors is better understood, we remain desperately impotent in our efforts, but may in some measure lower the frightful mortality by urging cooperation of the pediatricians, correlating all available clinical data and utilizing the now quite exact urological and roentgenographic facilities in all abdominal masses suspiciously renal in children.

Dr. Long (closing).—It is very important that we recognize this condition early and treat it immediately. I should like to emphasize again the importance of x-ray therapy which, at this time, may be the key to the solution of curing this type of disease by shrinking it to the point where it becomes operable. It is not entirely unlikely that at some time in the near future, with the further understanding and development of x-ray therapy, this may constitute the entire treatment.

A METHOD OF APPLICATION OF SKELETAL TRACTION FOR TREATMENT OF CONTRACTURE OF THE KNEE*

By D. H. O'Donoghue, M.D.†
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The problem of the knee with contracture has been a perennial one in all orthopedic clinics from their inception. There has been a multitude of approaches to this problem, which in itself is some indication of the lack of any ideal method of correcting contracture of the knee which is applicable to all cases. It is not, in my opinion, necessary to recapitulate the long list of appliances which have been devised for this purpose. Suffice it to say that they are excellent and serve their purpose well. The idea I am advancing here is not particularly new in principle, but it does present some new features in technic.

It is well recognized that the major obstacle to successful reduction of knee contracture is very often the tendency toward posterior subluxation of the tibia on the femur, caused by the extreme contracture of the posterior capsule, popliteus muscle, and the hamstring muscles. To overcome this tendency, many procedures have been advanced, such as posterior tenotomy, posterior capsulotomy, osteotomy of the femur, to mention a few operative procedures. On the conservative side, there are the various appli-

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†Assistant Professor of Orthopedic Surgery, University of Oklahoma School of Medicine.

ances which push upward on the upper end of the tibia and downward on the lower end of the femur. One of the best methods of application of this principle is application of linear traction on the leg, with vertical traction attached under the upper end of the leg. Anyone who has tried this procedure by the ordinary method is well acquainted with the technical difficulties in maintaining such traction continuously without the complications of ulceration of the skin, disturbing of circulation, displacement of the lines of traction, etc. During the past several years, in connection with cases at the Crippled Children's Hospital, and elsewhere, I have utilized the method herein described, and have, in the great majority of cases, found it to be entirely satisfactory and with a minimum of complication.

Briefly, the method consists of the following steps. A Kirschner wire is inserted through the crest of the tibia at the proximal end. To this wire the ordinary tension bow is applied, and vertical traction is obtained by suspension to an overhead bar, in the usual manner. A Kirschner wire, or other type of pin, is inserted through the os calcis, traction bow applied, and traction applied horizontally on the lower end of the leg. The exact amount of weight applicable to each traction point must, of course, vary decidedly with the type of case and with the degree of tendency toward subluxation. The theory in general is to apply maximum traction vertically at the initiation of treatment. As flexion contraction is overcome, less weight is applied in a vertical direction and more in a horizontal direction, until, as the termination of the traction period approaches and the tibia is pulled well forward in relation to the femur, traction upward becomes minimum, or may be eliminated entirely. The cases herein described and illus-

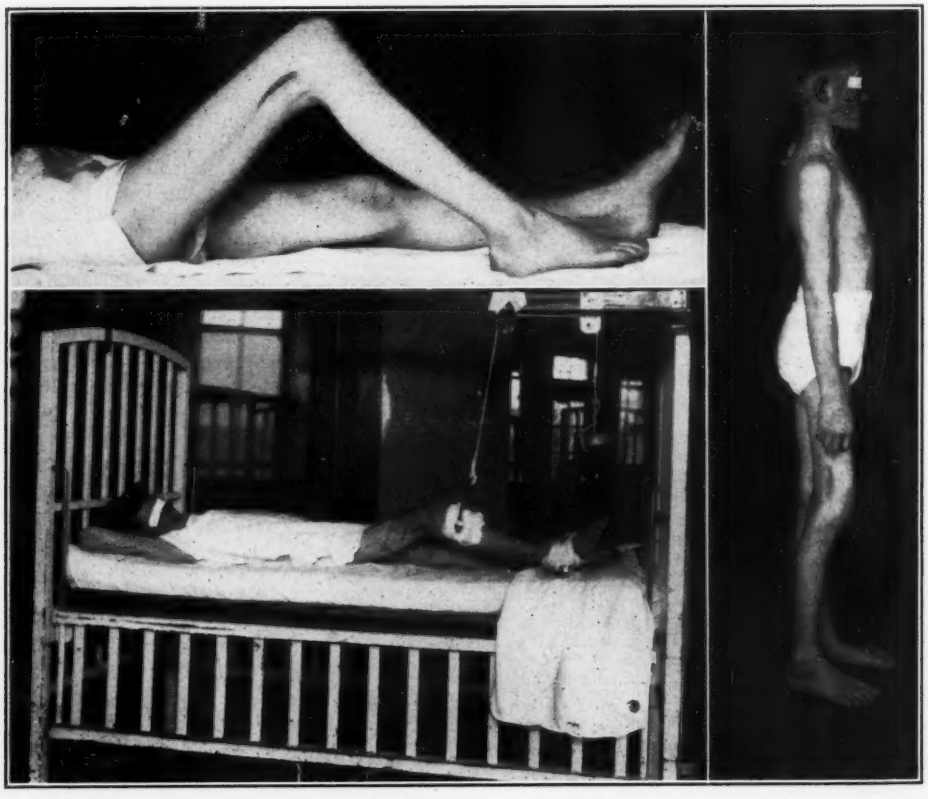

Fig. 1, Case 1

trated by photographs, are picked, not in sequence, but to illustrate the application of traction in the various types of contracture. Some of the cases in which we have found this to be particularly valuable are those of burn contracture with ulceration and loss of skin on the popliteal space, osteomyelitis of the femur with draining sinuses, and dense fibrous ankylosis of the knee following suppurative arthritis. In many cases of these types it has been extremely difficult to secure correction by the method of wedging casts, turnbuckle braces, or skin traction.

CASE REPORTS

Case 1.—L. C., a white boy, aged 13, was admitted to the hospital February 16, 1935. The diagnosis was osteomyelitis of lower end of right femur, contracture of knee and partial ankylosis of the patella of three years' duration. Examination revealed a draining sinus in the right lower femur, with range of motion from 90 to 115 degrees, with definite subluxation of the tibia on the femur. Double traction pins were applied March 20, 1935. April 19, 1935, the knee had been straightened to approximately 170 degrees, following which a cast was applied for three weeks, and a long leg brace ordered. (*Fig. 1, Case 1.*)

Case 2.—Y. T., a white girl, aged 16, was admitted to the hospital May 10, 1935. The diagnosis was multiple arthritis, and flexion contracture of both knees. The history dated back six years. She had had this flexion contracture ever since that time. Examination revealed contracture of the knees to 90 degrees. The hips were not limited. The feet were in good condition, but elbows ankylosed. May 20, 1935 double wire traction was applied to both legs. About August 7, 1935, the tibial pins were removed, at which time the knees had been straightened to about 170 degrees. August 15, the calcaneal pins were removed, and the knees would go completely straight. September 8, she was allowed up on leg braces with knees completely extended. (*Fig. 2, Case 2.*)

Case 3.—F. L., a white girl, aged 15, was admitted to the hospital October 4, 1935. The diagnosis was Still's disease. She had a typical history running back ten years, with involvement particularly of the knees and hands, and contracture of the knees lasting many years. Physical examination reveals 100 degrees contracture of both knees. Double skeletal traction was applied September 8, 1935, and removed December 13, 1935. Shortly after, the knees being entirely straight, she was fitted with long leg braces and discharged from the hospital walking. Later she returned to the hospital saying she

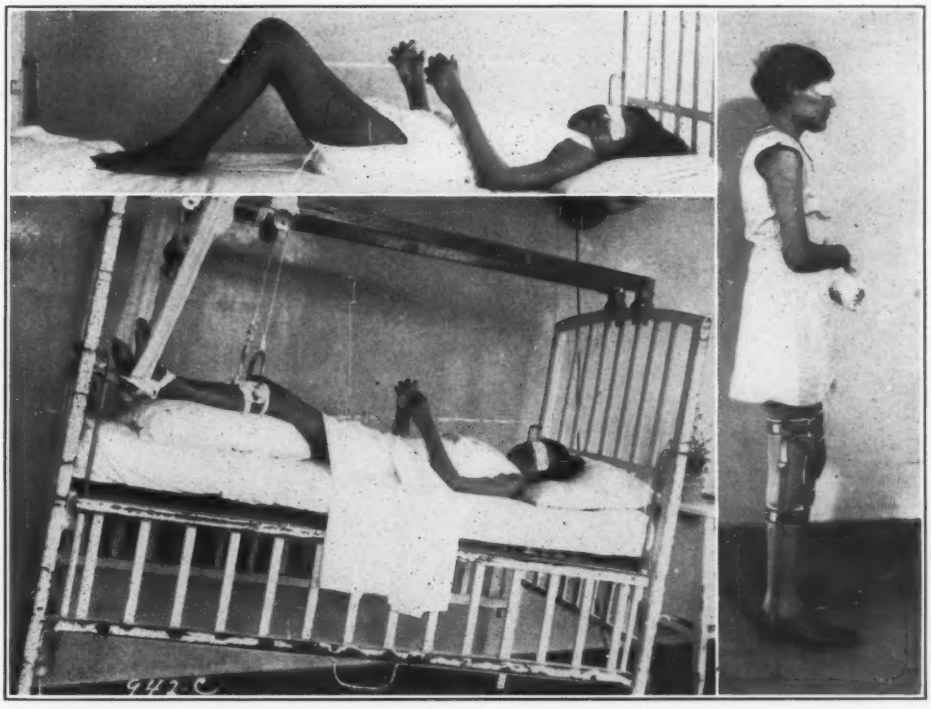

Fig. 2, Case 2

could walk alone with the aid of braces. (*Fig. 3, Case 3.*)

Case 4.—H. H., a white boy, aged 18, was admitted to the hospital February 18, 1935 because of a contracture of the right knee following an ax wound the year before. There was a suppurative arthritis and ankylosis of the patella. At the time there was 30 degrees motion in the knee, from 80 to 110 degrees. Double traction was applied February 22, 1935. Double traction was removed May 20, at which time he could extend to about 170 degrees, and flex to about 90 degrees. (*Fig. 4, Case 4,* illustrating change of weights).

Case 5.—E. C., a white boy, aged 8, was admitted to the hospital December 5, 1934. The diagnosis was osteomyelitis of the left femur with contracture of the left knee. Examination revealed a draining sinus of the lower left femur, and knee contracture to 120 degrees. December 12, 1934, double traction wires were applied with a single rope and weight. (*Fig. 5, Case 5.*) There was not much change after one week so separate weights were applied. December 29, 1934, the knee was entirely straight. January 9, 1935, sequestrectomy of the lower femur was done and a hip spica applied.

Case 6.—J. A., a white woman, aged 21, was re-admitted to the hospital October 31, 1934, for treatment of a contracture deformity resulting from a transverse myelitis. On admission she was still spastic with marked flexion contracture of the knee and hip. She had 90 degrees flexion contracture of the left knee. November 7, the Soutter operation for contracture of the hip was done. February 10, 1935, nerve section to hamstrings was done, and tenoplasty of the heel cord, at which time traction was removed, and the knee was completely straight. Subsequent to this time she was able to walk. (*Fig. 6, Case 6.*)

Case 7.—L. B., a white girl, was admitted to the hospital September 29, 1936. The diagnosis was angioma of the right leg with contracture of the knee. The angioma was congenital, the contracture of nearly four years' duration. She was referred to the orthopedic service November 6, 1936, at which time examination revealed flexion contracture of the knee. The lesion of the leg was benign, so we thought it reasonable to attempt to obtain a functional joint. Double traction was applied November 23, 1936. About a week later the pin pulled out of the tibia and was replaced November 30. December 5, she could extend her knee to 130 degrees. December 13, she could extend to 160 degrees. January 11, 1937, traction was removed, at which time the contracture of the knee and hip were practically corrected. February 9, 1937, she was walking in a brace with the knee straight. (*Fig. 7, Case 7.*)

Case 8.—A. B., a white girl, aged 11, was admitted to the hospital June 22, 1935. The diagnosis was osteomyelitis of the upper tibia of several months' duration with contracture of the knee to 90 degrees. She was

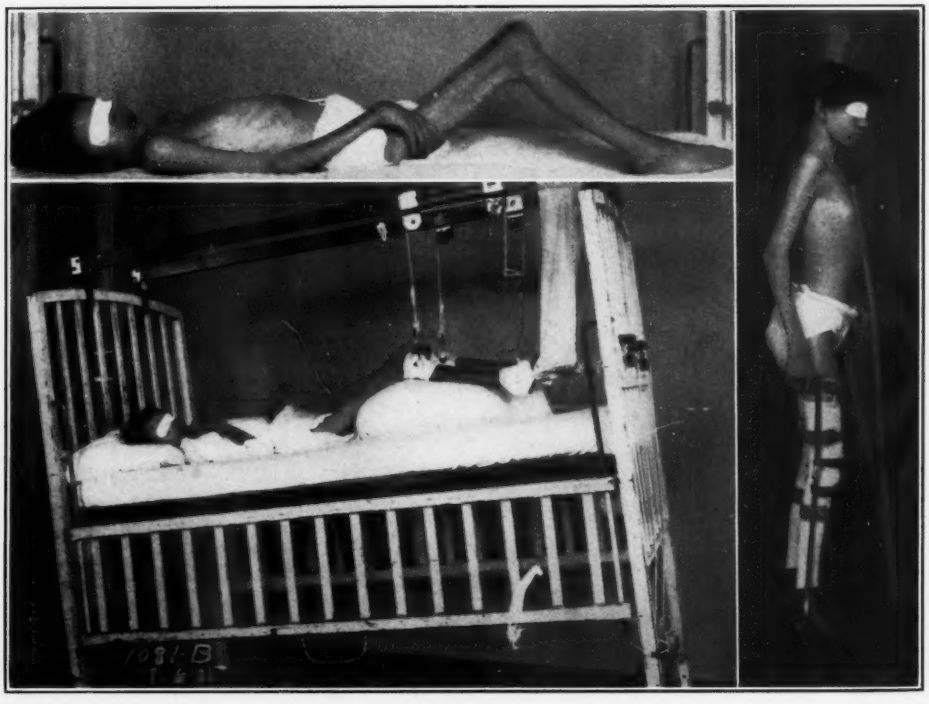

Fig. 3, Case 3

operated upon for osteomyelitis, with no treatment for knee contracture. Osteomyelitis treated in the usual manner. She was re-admitted September 7, 1935 for treatment of the contracture, at which time she still had a large ulcerated wound at the upper end of the tibia and a pathologic fracture of the tibia healed with posterior angulation. Traction was applied October 8, 1935, at which time the contracture was to 75 degrees. November 7, the contracture was to 150 degrees. December 18, she had extension to 165 degrees, at which time a plaster cast was applied. (*Fig. 8, Case 8.*)

Case 9.—B. D., a white boy, aged 17, was re-admitted to the hospital for contracture of the knee following suppurative arthritis. Knee contracture was about 90 degrees. X-ray revealed bony ankylosis of the patella and subluxation of the tibia. Traction was applied April 3, 1935. The following two weeks the patient became uncooperative, resting his foot against the foot of the bed, lifting weights and doing everything possible to interfere with correction. He complained bitterly of pain. The pins were removed April 15, 1935, and ad-

Fig. 5, Case 5

Fig. 4, Case 4

Top—Fig. 6, Case 6
Bottom—Fig. 7, Case 7

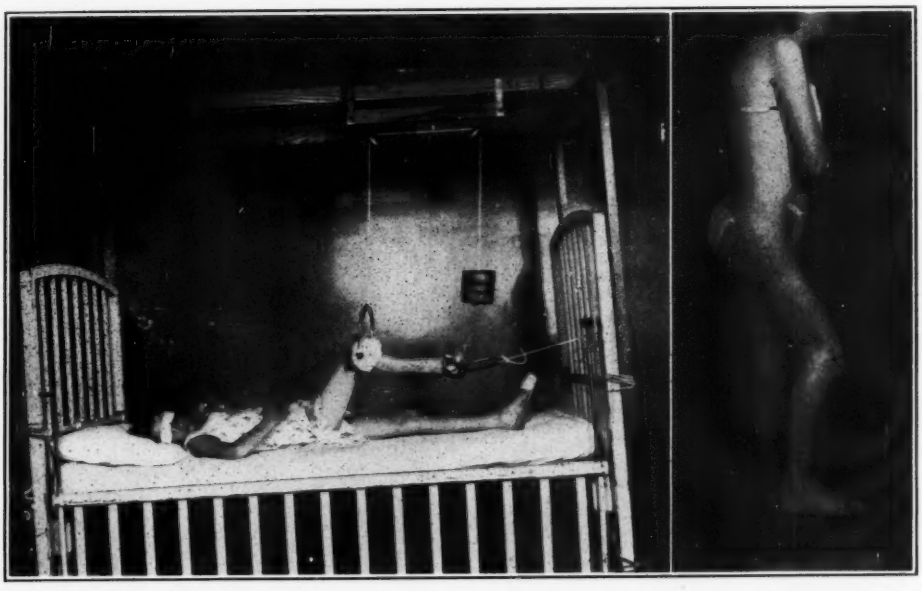

Fig. 8, Case 8

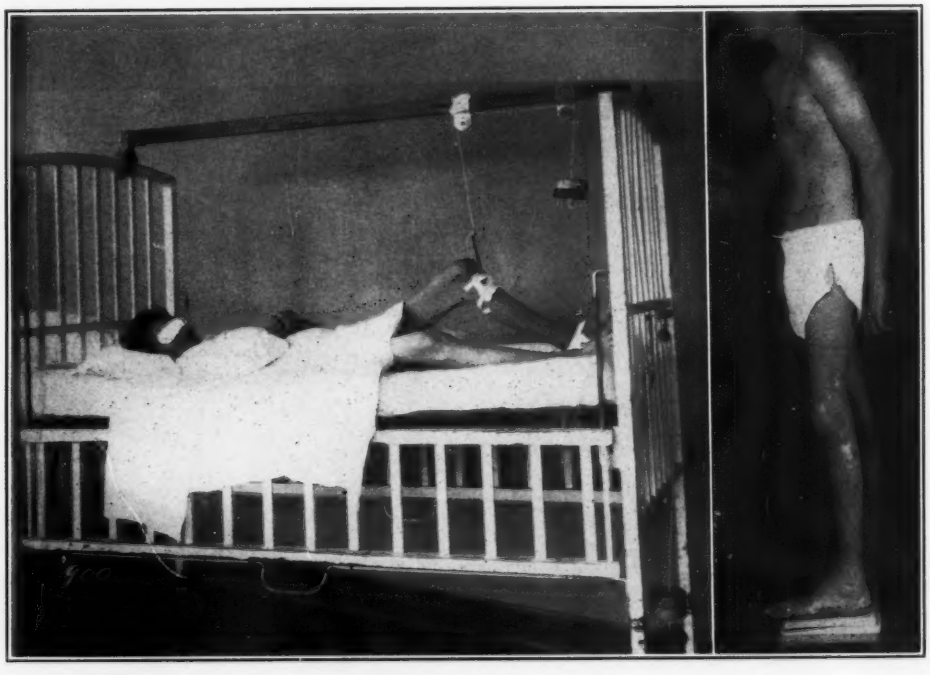

Fig. 9, Case 9

hesive traction applied. The patient was still uncooperative. He was put in a Campbell extension knee brace which was completely unsuccessful because he would loosen the screws. He was put in a turnbuckle support with such severe complaints that it had to be removed. Finally he was placed in a double hip spica with turnbuckle which we were able to lock. This time he broke the rivet on the turnbuckle. Finally failing in all methods, on November 1, 1935, operative fusion was done. (*Fig. 9, Case 9.*)

SUMMARY

Among the many cases treated by this method, there have been surprisingly few complications. One case was of osteomyelitis of the lower femur, with marked destruction of bone, which resulted in a low-grade osteomyelitis around the pin site at the upper end of the tibia, and which healed promptly without serious complications. Another case was a boy about eighteen, who was extremely uncooperative and refused to have the traction constantly applied. In *Case 9* the method was a total failure and correction was obtained by operative fusion. In the great majority of cases, the reaction of the tissue to the traction wire is similar to that obtained in using skeletal traction elsewhere. In no case has there been a persistent sinus which refused to heal.

CONCLUSION

There have been remarkably few complications and no unfortunate sequelae in the many cases treated by this method. It adds to the comfort of the patient and minimizes the problem of nursing care. This technic is presented not as a panacea, but as a method which has been, in many instances, a useful adjunct to the treatment of the contracted knee.

MUCOID CARCINOMA OF THE BREAST*

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Mucoid, colloid or gelatinous carcinoma of the breast is a relatively rare neoplasm. Its incidence is uniformly given by various authors as 1-3 per cent of all breast carcinomas. In 2944 breast carcinomas collected by Gaabe[1] there were 49 gelatinous carcinomas or 1.66 per cent. In reviewing 950 cases of breast carcinoma examined in the Johns Hopkins Hospital between 1889 and 1931, Lewis and Reinhoff[8] found 12 (1.3 per cent) gelatinous carcinomas. Deaver and McFarland [2] found 10 cases (1.73 per cent) in their study of 575 breast cancers. Lee, Hauser, and Pack[9] of the Memorial Hospital discovered 30 of these tumors in a histological review of 1922 cases. Illingsworth and Dick[10] state that small areas of mucoid degeneration are not uncommon in mammary growths, and that occasionally this change is sufficiently obvious to merit separate description. By the study of serial sections of whole breasts Cheatle and Cutler[6] have demonstrated that small areas of mucoid degeneration are not infrequent.

Mucoid carcinoma occurs, on an average, at a slightly later age period than the more common types of breast carcinoma. In Geschickter's[12] series the peak of age incidence was between 46 and 50 years as compared to a peak of between 41 and 45 years for the other types of cancer of the breast. The average age for gelatinous carcinoma in the Memorial Hospital series was 52 years and that for the more common carcinomas 51 years.

The clinical features of this tumor are of interest, and at times may enable one to make a preoperative diagnosis. The first sign noted by the patient is usually a painless, slow growing lump in the breast. The large size of some of these tumors has been emphasized by many observers. Ewing[4] states that the mucoid tumors reach the largest dimensions of any mammary carcinomas. The nipple shows no change for a long period of time, after which it may be pushed outward or enlarged instead of retracted as in other types of breast cancer. A bloody discharge from the nipple is sometimes present. This was noted in 10 per cent of Geschickter's 83 cases. Discoloration and ulceration of the skin are seen much later than in the more common mammary cancers and usually occur in association with the larger tumors. An area containing mucoid material may rupture through the skin and give rise to a persistent sinus discharging mucin. The late metastases of these tumors constitute a striking feature. Olch[7] makes the statement that the general course of mucoid carcinomas is about three times longer than the other types, both in rate of growth, and in rate of metastasis.

The diagnosis of these tumors is well discussed by Geschickter. He emphasized four principal

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clinical features: (1) the relatively small size of the tumor in comparison with the long duration of symptoms; (2) protrusion and enlargement of the nipple on the affected side; (3) cystic character of the growth on palpation; (4) Halstead's sign: the feeling of a "swish" on firm pressure. The chief point in differential diagnosis is, of course, the differentiation from a benign cyst, which may be ruled out by aspiration.

It is generally accepted that these tumors are of low grade malignancy; however, it is well known that an occasional one may be highly malignant. Shepherd[11] states that gelatinous carcinoma is of low grade and easily cured by radical excision.

The pathological features of mucoid carcinoma are characteristic. The gross appearance varies according to the amount of mucoid degeneration. In the advanced state the entire tumor may consist of gelatinous material, but in the earlier stages gelatinous material is seen only in isolated portions of the tumor, and, in some instances, may not be discernible on gross examination. The pure mucoid carcinoma may or may not be encapsulated. Its cut surface reveals a translucent gelatinous material throughout. The color of this material varies according to its vascularity and the presence or absence of degenerative changes and hemorrhage. The pure gelatinous substance is light greenish gray or yellow, but if hemorrhage occurs, it assumes a dull brown color. The tumors are often intersected by numerous fibrous trabeculae, producing a honey-combed appearance. Cystic cavities of varying size are common and these may contain old blood.

The microscopic picture also varies with the amount of mucoid degeneration. In the carcinoma with advanced mucoid degeneration the epithelial elements are few and scattered. There are small nests of epithelial cells separated by a loose stroma filled with mucin. These nests may be solid or may show definite gland formation, depending on the type of the original tumor. The appearance of the cells may vary considerably. Some contain transparent droplets of mucin in their cytoplasm while others are distended with this material which pushes aside the nuclei giving the typical signet ring appearance. Still others show disintegration of the cytoplasm, and in some instances, only the nuclei or fragments of the degenerating nuclei remain. In the cells which show the least degenerative change the nuclei appear hyperchromatic and mitoses are occasionally seen.

The appearance of those carcinomas in which the mucoid material is deposited in isolated foci or sparsely scattered throughout the solid tumor depends almost entirely on the type of carcinoma involved in the degenerative change. The types most often involved are the bulky adenocarcinoma, intracystic papillary carcinoma, duct carcinoma and scirrhous carcinoma. In the case of mucoid degeneration these tumors will have their typical histology, but in some areas the epithelial cells will show the changes described above and the stroma will contain a large amount of pale staining mucin.

The origin of the mucoid material has long been a debated question. As stated by Reel,[3] Lee, Hauser and Pack, and Kaufmann,[5] the material may arise either from epithelium or connective tissue; however it is probable that it is usually epithelial in origin.

Fig. 1, Case 1
Mucoid carcinoma of the breast. Right breast. In the upper and outer quadrant is seen the incised tumor with its crater-like cavity partly filled with gelatinous material and blood. The nipple is not involved (photograph).

The treatment of mucoid carcinoma is surgical. The tumor is radioresistant, and the best hope of cure lies in radical and early excision.

REPORT OF CASES

Case 1.—C. McB., a negro woman, aged 35 years, was admitted to the surgical service of Dr. J. H. Francis at the John Gaston Hospital, April 8, 1932, complaining of a gradually enlarging tumor mass of one year's duration in the upper and outer quadrant of the right breast. One week before admission the mass had become very painful. There was no history of discharge from the nipple.

Physical examination revealed a well developed and nourished negro woman. The right breast was enlarged and there was a firm mass about the size of a small orange in the upper and outer quadrant. Near the center of this mass there was a small area which was slightly fluctuant. The skin overlying the mass was fixed. The nipple was not affected by this mass. The axillary lymph nodes were moderately enlarged and firm, but not tender.

A radical mammectomy was done and an uneventful postoperative course followed.

Pathologic Report.—The specimen consisted of the right breast, a portion of the pectoralis muscles, and several axillary lymph nodes. The upper and outer quadrant of the breast was the seat of a moderately firm tumor mass approximately 8.5 cm. in diameter. The skin overlying this tumor was fixed and the central portion of the mass was softened. There was no involvement of the nipple (*Fig. 1*). Section through the tumor mass revealed a large crater-like cavity measuring 6.5 cm. in diameter immediately beneath the skin. This cavity was partially filled by a translucent gelatinous material into which considerable hemorrhage had occurred. The floor of the cavity was composed of a fairly well circumscribed zone of greenish gray, translucent material which

Fig. 2, Case 1

Mucoid carcinoma of the breast. Right breast, left half, on section. The gelatinous material and blood extends into the wall of the crater-like cavity, and passes over into a firm, grayish white, granular tissue which infiltrates breast and muscle (photograph).

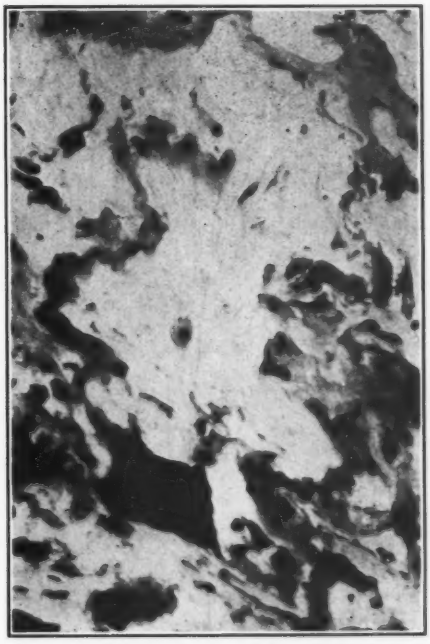

Fig. 3, Case 1

Mucoid carninoma of the breast. Partly degenerated masses of carcinoma cells are seen surrounded by a large amount of stringy mucin, separated by a delicate fibrous tissue stroma (photomicrograph x 300).

extended into the breast tissue on all sides of the cavity. Beneath this translucent, gelatinous material there was a firm, grayish white, granular tissue which was infiltrating the surrounding breast tissue as well as the attached muscle (*Fig. 2*).

The lymph nodes were slightly enlarged and the capsule was under tension. On section, they appeared pink and translucent.

The greater portion of the microscopic sections showed numerous small irregular masses, strands and columns of hyperchromatic epithelial cells separated by large amounts of pale blue, stringy, mucoid material, held in place by a delicate, fibrous tissue stroma. Numerous red blood cells were often seen in the mucoid material. The cytoplasm of many of the epithelial cells was swollen and distended with mucin. Some areas near the periphery of the mass were very cellular, and closely resembled the typical medullary carcinoma. In these mitotic figures were fairly frequent, but in the areas of marked mucoid degeneration evidences of cell proliferation were practically absent (*Fig. 3*). The lymph nodes showed some hyperplasia but no metastatic carcinoma.

Case 2.—J. G., a negro woman, aged 61 years, was admitted to the surgical service of Dr. Ernest Kelly at the John Gaston Hospital, October 3, 1934, complaining of a tumor in her left breast. The tumor mass was first noticed 4-5 months before admission. It grew progressively larger and 2½-3 months before admission it became ulcerated. There was no history of discharge from the nipple. The past history gave evidence of long-standing diabetes.

Physical examination revealed a well developed, poorly nourished, dehydrated negro woman. The left breast was enlarged and there was an ulcerated, fungating tumor mass approximately two inches in diameter in the upper and outer quadrant. The axillary lymph nodes were palpable but not tender.

A simple mammectomy was done October 4, 1934. The postoperative course was uneventful.

Pathologic Report.—The specimen consisted of the left breast. In its upper and outer quadrant there was a fungating, cauliflower-like mass 6 cm. in diameter projecting above the skin surface. In its central portion there was a deep crater-like ulcer. The floor of the ulcer

Fig. 4, Case 2

Mucoid carcinoma of the breast. Left breast, right half. Projecting through the skin of the upper and outer quadrant is the fungating, cauliflower-like, ulcerated tumor with its gelatinous base. The uninvolved nipple is on the right, below (photograph).

Fig. 5, Case 2

Mucoid carcinoma of the breast. Left breast, right half, on section. The gelatinous tissue is infiltrating the underlying breast tissue and extending to a greater distance as larger masses, below. The normal nipple is seen on the left (photograph).

was dark red and very translucent (*Fig. 4*). Section through the base of the ulcer revealed a homogeneous, yellowish, translucent mass which was fairly well circumscribed, but extended well beyond the margins of the ulcer into the underlying breast tissue, and to a depth of approximately 2.5 cm. below the skin surface. Several detached masses were seen deeper in the breast and the lesion was some distance from the normal nipple. (*Fig. 5*).

Microscopic sections showed varying degrees of mucoid degeneration. In some areas there were masses of hyperchromatic epithelial cells, showing definite glandular arrangement, which were surrounded by hyalinized fibrous tissue, but the predominant feature was the presence of large areas showing small irregular masses of epithelial cells separated by a large amount of pale blue, stringy mucoid material in which irregular remnants of pink staining hyalinized fibrous tissue were seen. The epithelial cells in these regions were often markedly distorted, and their cytoplasm distended with mucin. The nuclei were hyperchromatic, but mitotic figures infrequent (*Fig. 6*).

Case 3.—B. A., a negro woman, aged 48 years, was admitted to the surgical service of Dr. J. L. McGehee at the John Gaston Hospital, March 11, 1936, complaining of a rapidly growing tumor mass of four months' duration in the right breast. There was a history of bloody discharge from the nipple two months before admission. She had received preoperative x-ray therapy.

Physical examination revealed a moderately firm, rounded tumor mass approximately 8 cm. in diameter in the upper and outer quadrant of the right breast. The skin overlying this mass was slightly fixed, and there was a slightly greater elevation to the nipple than normal. The axillary lymph nodes were enlarged and firm but not tender.

A radical mammectomy was done March 12, 1936, and the postoperative course was uneventful.

Pathologic Report.—The specimen consisted of the right breast, a portion of the pectoralis muscles and several axillary lymph nodes. The upper and outer quadrant of the breast contained a tumor mass measuring approximately 6 cm. in diameter. The skin overlying this mass was fixed and nodular and there was some swelling and prominence of the nipple. Sectioned surface of the breast revealed a rounded tumor rich in translucent, gelatinous material which was greenish gray to dark reddish brown in color. The tumor was intersected by numerous fibrous trabeculae which gave to it a honeycombed appearance. It was well circumscribed and encapsulated. The gelatinous material had extended into and distended the lumen of a duct of the nipple.

The lymph nodes were enlarged and tense. On section

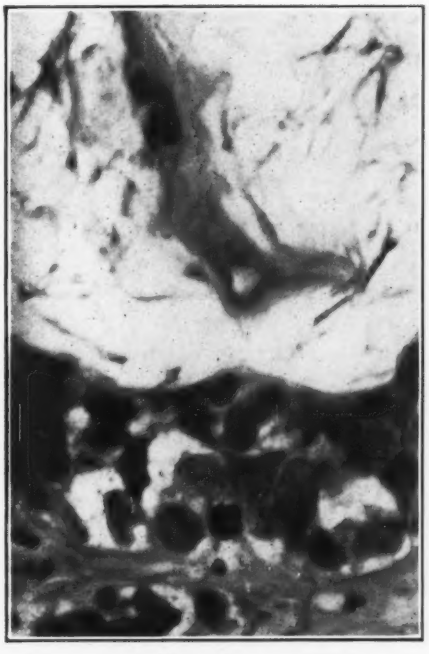

Fig. 6, Case 2

Mucoid carcinoma of the breast. Note the mucin distended epithelial cells with large pale nuclei occurring in irregular mass formation, associated with a large area of stringy mucoid material, held together by a small amount of hyalinized fibrous tissue (photomicrograph x 725).

Fig. 7, Case 3

Mucoid carcinoma of the breast. Right breast, right half, and axillary lymph nodes on section. Breast shows in upper and outer quadrant an encapsuled, honey-combed, gelatinous tumor, with bulging areas under the skin and extension in a duct to the nipple. Lymph nodes are enlarged and present a similar appearance (photograph).

Fig. 8, Case 3

Mucoid carcinoma of the breast. Capsule is shown containing mucoid material surrounding masses of carcinoma cells. A capillary is seen above and to the right (photomicrograph x 300).

they revealed a honey-combed structure with the translucent, gelatinous material in the meshes of the stroma. Some showed central cyst formation (*Fig. 7*).

The microscopic picture was that of a duct carcinoma in which mucoid degeneration had occurred. There were numerous large rounded alveolar-like masses of epithelial cells which in most regions were surrounded, or at least partially surrounded, by poorly stained mucoid material. The epithelial cells were large and pale and the cytoplasm was distended with mucin. There was slight variation in the size and shape of the cells. Mitotic figures were relatively few in number. Sections from the periphery of the mass revealed a thin hyalinized fibrous capsule which was apparently not invaded by the tumor cells (*Fig. 8*). The lymph nodes showed an histologic appearance similar to that of the primary tumor, consisting of mucoid degenerating carcinoma cells arranged in irregular masses, poor in mitotic figures, but associated with large accumulations of mucoid material.

SUMMARY AND CONCLUSIONS

An attempt has been made to give a concise review of the clinical and pathologic features of mucoid carcinoma of the breast. Three cases have been reported. The first of these was a medullary carcinoma in which mucoid degeneration had occurred. The second was an adenocarcinoma and the third a duct carcinoma. The clinical features in these three cases were those of malignancy, but they did not suggest a preoperative diagnosis of mucoid carcinoma. The pathologic features were characteristic and the histological picture indicated a low grade of malignancy.

We are inclined to believe that the clinical features of mucoid carcinoma are not diagnostic, unless the tumor has grown through the skin and sinuses discharging mucin are in evidence. The pathologic picture, on the other hand, is quite characteristic.*

BIBLIOGRAPHY

1. Gaabe, cited by Kaufmann.5
2. Deaver, J. B.; and McFarland, J.: The Breast: Its Anomlies and Diseases and Their Treatment, p. 485. Philadelphia: P. Blakiston's Sons & Co., 1917.
3. Reel, P. J.: Gelatiniform Carcinoma of the Breast. Ann. Surg., **73**:108-110 (Jan.) 1921.
4. Ewing, J.: Neoplastic Diseases, Ed. 3, p. 552. Philadelphia: W. B. Saunders Company, 1928.
5. Kaufmann, E.: Pathology for Students and Practitioners, translated by S. P. Reimann, **3**:1794-1798. Philadelphia: P. Blakiston's Sons & Co., 1929.
6. Cheatle, L. G.; and Cutler, M.: Gelatinous Carcinoma of the Breast. Arch. Surg., **20**:569-590 (April) 1930.
7. Olch, I. Y.: The Diagnosis of Diseases of the Breast. Graham, E. A.: Surgical Diagnosis, **3**:211-326. Philadelphia: W. B. Saunders Company, 1930.
8. Lewis, D.; and Reinhoff, W. F.: Cancer of the Breast. Ann. Surg., **95**:336-400 (March) 1932.
9. Lee, B. J.; Hauser, H.; and Pack, G. T.: Gelatinous Carcinoma of the Breast. Surg., Gyn. and Obst., **59**:841-857 (Dec.) 1934.
10. Illingsworth, C. F. W.; and Dick, B. M.: A Textbook of Surgical Pathology. Ed. 2, p. 367. London: J. & A. Churchill, 1935.
11. Shepherd, W. F.: Carcinoma of the Breast, Arch. Surg., **37**:190-210 (Aug.) 1938.
12. Geschickter, C. F.: Gelatinous Mammary Cancer. Ann. Surg., **108**:321-346 (Sept.) 1938.

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*We are indebted for the illustrations in this study to Dr. Joseph L. Scianni, artist, University of Tennessee, Pathological Institute.

DISCUSSION (*Abstract*)

Dr. Wm. H. Bailey, Oklahoma City, Okla.—The term "mucoid" carcinoma is now used to classify a certain group of breast tumors which were formerly called "colloid" carcinoma by the older authors. The breast is not the only organ in which this type of cancer develops. Other locations in which mucoid carcinoma is found are the stomach and other parts of the digestive tract and in the bronchi.

Boyd and other authors consider this particular type of tumor a mucoid degeneration of an already pre-existing carcinoma. Some tumors, however, appear to show this type of tissue from their beginning. Still others show the mucoid type of cell in one or more areas, while the remaining tissue gives the picture of the usual malignant cell. Although this tumor has several distinctive characteristics which assist in its identification, it probably is not a separate type of carcinoma. The same factors that cause the mucoid material to develop may also bring about its other characteristics.

Although this tumor may show rather rapid growth,

this is probably due more to the swelling of the cells rather than to an increase in their number.

An interesting fact in regard to this tumor is that secondary metastatic nodules developing in other parts of the body very often show the same type of mucoid degeneration. This would make it seem probable that the cause of this mucoid degeneration is a factor outside of any local condition in the particular environment in which the original tumor developed, possibly a systemic reaction.

Dr. Schmeisser (closing).—It is true that the mucoid carcinoma represents only a degenerative change in other types of carcinoma; but the biological factor which is responsible for the mucoid change is also responsible for other profound biological changes, expressing themselves in a carcinoma which grows very slowly, becomes unusually large, infiltrates slowly and metastasizes late, if at all. This is what makes the mucoid carcinoma of the breast interesting and, therefore, the present study has been made.

PALATAL MYOCLONUS*

A CLINICAL AND ANATOMICAL REPORT OF TWO CASES

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The syndrome of palatal myoclonus, described by Pollitzer many years ago, has not attracted great attention from the English and American neurologists[1] though in Europe, German, and especially the French authorities,[2 3 4] have reported a large number of cases. In some of the reports the structural changes responsible for the syndrome have been identified, and an attempt made to elucidate its significance from the neurophysiologic standpoint.

We have recently had the good fortune of an opportunity to study the brains of two patients who showed the palatal myoclonus syndrome. These specimens were sectioned in the laboratory of the Henry Phipps Psychiatric Clinic and we wish to acknowledge our gratitude to Dr. Adolf Meyer and Miss Cecelia Bisson for permission to use this material. The present investigation was from the postmortem standpoint, but it is to be regretted that the clinical records are rather inadequate. The patients showed signs of other defects of the central nervous system. In both cases we have been able to demonstrate the lesions responsible for these signs and symptoms.

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*From the Subdepartment of Neurology, the Johns Hopkins University and the Medical Division of the Baltimore City Hospitals.

CASE REPORTS AND ANATOMICAL FINDINGS

Case 1.—A patient of 66 with arteriosclerosis had an illness of apoplectic onset producing weakness and ataxia of the right extremities. Later bilateral myoclonic movements of the perioral muscles, palate, pharynx and diaphragm were observed. Softening involved the whole right half of the cerebellum. There were degenerative changes in the opposite inferior olive.

M. B., (B.C.H. 20484), a white woman of 66 years, was admitted to the Baltimore City Hospitals on November 10, 1932. She gave a story of falling on the street a few hours before admission. Unconsciousness lasted only a few minutes. She was able to walk but complained that her right arm and leg were weak. Examination elicited some apparent loss of strength in the right extremities but no spasm or rigidity were found. The deep reflexes were active and equal on both sides. No Babinski reflex was obtained. The patient swayed in Romberg's position. The right knee joint was enlarged and relaxed. In the hospital the patient's course was uneventful until, in the spring of 1933, rhythmic movements of the palate were discovered and she was re-examined.

The patient seemed well nourished and physically well preserved but a mental defect prevented her full cooperation in the examination. The lungs showed signs of severe emphysema and a moderate amount of kyphosis was noted. The heart was not enlarged and no murmurs were noted on auscultation. The rhythm was regular. The peripheral vessels were much thickened and could be rolled under the finger easily. There was edema of the ankles. The blood pressure was 205/124.

Nervous System.—The pupils were round and equal. They reacted to light and accommodation. The retinal vessels showed arteriosclerosis but the optic discs were normal. Extra-ocular movements were full and a lateral nystagmus was brought out on looking to the right. The head showed a nodding tremor and the corners of the mouth were seen to be in rhythmical contraction. The uvula was in constant rhythmical motion at a rate of 120 per minute. The pulse rate was about half this rate at the time of examination. Laryngoscopic study demonstrated that the contractions were also present in the pharyngeal wall, the ostia of the eustachian tubes, the muscles of the floor of the mouth, and those attached to the hyoid bone.

The right arm and leg showed weakness. The heel-knee and finger-nose tests were performed poorly on the right side. The abdominal reflexes could not be shown. The deep reflexes were hyperactive on the right side. Fluoroscopy demonstrated that the myoclonic movements were present bilaterally in the diaphragm. It was not possible to perform a reliable examination of sensation. The Wassermann reaction was negative in the blood and other laboratory examinations gave no information of significance. The patient died on April 12, 1934.

Autopsy Report.—Examination of the brain immediately disclosed the character of the abnormality. There was almost a complete softening of the right half of the cerebellum. Study of the sections (*Fig. 1*) showed that the loss of structure extended dorsally almost to the midline. Laterally the flocculus and a small portion of the hemisphere were preserved. This hemisphere was cut off from its connection with the brain stem. The dentate nucleus was almost completely destroyed on the

right; there were only a few cells of the lateral portion of the nucleus remaining.

The corpus restiform was completely degenerated on the right and the same was true of the brachium conjunctivum (*Fig. 3*). On the same side the fibers of the brachium pontis were cut off and degenerated at the lateral edge of the pons.

There was total degeneration of the inferior olive and the accessory olives on the left (*Fig. 1*); the changes had the appearance of "pseudohypertrophy." Only a few cells remained. Many of them were shrunken and a few showed eccentric nuclei and swollen cytoplasm. The olivo-cerebellar fibers were completely degenerated at the hilus of this olive and at the point where they normally cross the midline to join the opposite corpus restiform. The central tegmental fasciculus or thalamo-olivary tract appeared normal on both sides (*Fig. 2*). The capsule of the left red nucleus was lost (*Fig. 2*) and there were few myelinated fibers in the substance of the nucleus.

There was some degeneration of the left pyramidal tract; the right appeared quite normal. The degeneration involved the mesial portion of the left crus in the region of the fronto-ponto-cerebellar pathway.

Case 2.—A patient of 61 with arteriosclerosis developed a right hemiplegia and, later, weakness of the left side of the body. Myoclonic movements of the palate and larynx were observed on the right side. There was degeneration of the lateral portion of the right dentate nucleus and of the superior portion of the left inferior olive.

P. M. (Baltimore City Hospitals, 6372), a colored man of 61 years, was admitted on the second of August, 1934, with the complaint of weakness in his legs and difficulty of speech.

Investigation of his family and past history gave no information of value. The present illness was said to have begun about three years before with a sudden paralysis of his right arm and leg. Consciousness was

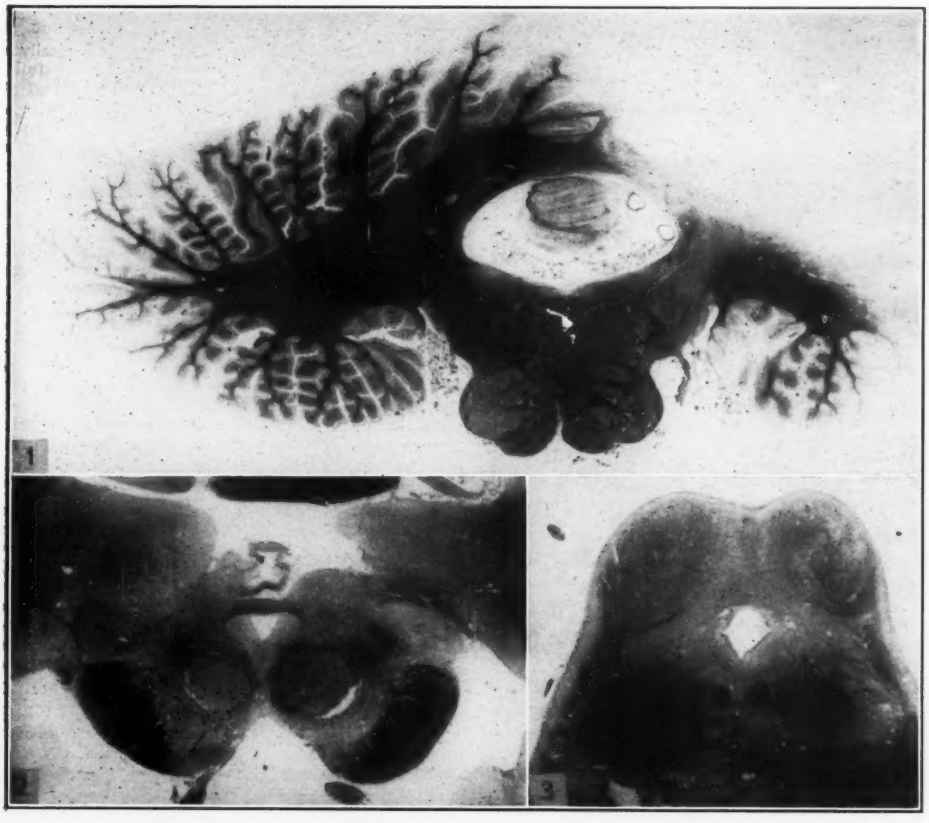

Fig. 1. Massive degeneration of the right cerebellar cortex. "Pseudohypertrophic" condition of the left inferior olive. The inferior cerebellar peduncle does not stain on the right side.

Fig. 2. Loss of the capsule of the left red nucleus and the nucleus itself is small.

Fig. 3. Section at level of the acoustic colliculi showing loss of the right superior cerebellar peduncle.

not lost at this time but the patient stated that he had difficulty of articulation. He subsequently recovered some use of his arm and leg, but was obliged to use a cane and could not resume work. For about a month before coming into hospital his legs had been growing progressively weaker and the speech difficulties increasing. During this period he had difficulty in swallowing, but at no time had he nasal regurgitation. For four days before admission he had been unable to stand.

His temperature was 99° F, and pulse, 68. The blood pressure varied during hospitalization from 220/110 to 160/110. The patient was a well developed colored man who did not seem acutely ill. Examination of the lungs showed signs of a moderate degree of emphysema. The heart was somewhat enlarged but auscultation revealed no cardiac murmurs. The peripheral arteries were very much thickened and tortuous.

Nervous System.—The pupils were slightly irregular but reacted well to light and accommodation. Ophthalmoscopic examination showed marked retinal arteriosclerosis. The extra-ocular movements were full; the right palpebral fissure was wider than the left. There was a definite weakness of the right lower facial musculature. The muscles forming the right side of the palatal arch were in constant movement at a rate of about 160 per minute. The pulse rate at this time was 68 per minute. The muscles at the base of the tongue on the right side also showed a rhythmical contraction. Laryngoscopic examination revealed that the right vocal cord shared in the clonic movements and the posterior pharyngeal wall moved to the right on palatal contraction. The tongue had a coarse tremor and, on protrusion, deviated to the right side. There was a moderate loss of power in both arms and this was more marked on the right side. There was a tremor of the right arm and hand accentuated by voluntary movements. No muscular atrophy was seen in either the upper or lower limbs. Clonic contractions of the right arm, lasting for several minutes, could be easily produced upon flexion of the elbow or by tapping the triceps tendon. There was little muscular power in either lower limb. The gait, when the patient was supported, was spastic and shuffling. The finger-nose test demonstrated ataxia on the right side, and heel-knee ataxia was also present on this side. All tendon reflexes in the arms were brisk. Hoffmann's sign was noted on the right side. The abdominal reflexes could not be elicited. The knee and ankle jerks seemed overactive bilaterally. There was unsustained ankle and patellar clonus on the right side. The Babinski reflex was present on this side. Tests of the sensory functions showed no abnormalities save loss of vibratory sensation in the legs.

Laboratory Studies.—The Wassermann reaction was negative in the blood and spinal fluid. The hemoglobin, red and white cell counts were normal. The cerebrospinal fluid pressure was normal. No globulin or cells were present. Fluoroscopic examination revealed no myoclonic movements of the diaphragm.

The patient later developed fecal incontinence. Choking was troublesome, if he swallowed liquids rapidly. He died in November, 1935. At autopsy the cause of death was found to be a malignant tumor which was thought to arise from the gallbladder or bile ducts.

The brain of this patient showed a generalized atrophy of the cerebral cortex but no areas of softening were observed in the uncut brain. There was marked sclerosis of the large arteries at the base. The inferior olives were plainly visible on the surface of the medulla. There were many small areas of encephalomalacia scattered through the basal ganglia. The right side of the corpus callosum was atrophic. One area of softening damaged the descending fibers in the left internal capsule. The left corticospinal tract was almost destroyed (*Figs. 4* and *5*). Smaller areas of softening in the right internal capsule appeared to injure particularly the fibers of the fronto-ponto-cerebellar pathway. There were less marked changes in the right corticospinal tract. The whole right thalamus was diffusely shrunken.

In this patient the changes in the pathways whose injury produce palatal myoclonus were less marked than in the previous case. Only the lateral portion of the right dentate nucleus was swollen and "pseudohypertrophic" (*Fig. 4*).

The mesial and anterior portions of the nucleus seemed quite normal as observed with the eye and by microscopic study. The changes were quite sharply defined. There was a distinct loss of cells in the lateral area and an increase in glial tissue. The changes in the dentate nucleus appeared to be dependent upon sclerotic changes in the small arteries. The brachium conjunctivum was considerably decreased in size on the right.

The central tegmental fasciculi appeared normal on both sides. The anterior portion of the left inferior olive was distinctly abnormal (*Fig. 5*). There was a "pseudohypertrophy" of the nucleus in this region; the cells were shrunken except for a few with swollen cytoplasm and eccentric nuclei. The caudal portion of the inferior olivary nucleus and the accessory olives were quite normal.

Only a portion of the fibers in the hilus of the left nucleus was degenerated. The fibers decussating to join the right restiform body were reduced in number.

DISCUSSION

The onset and symptoms of palatal myoclonus seem to be rather similar in all cases; accessory abnormalities appear, due to involvement of other pathways. Thus cases showing pseudobulbar palsy or the syringobulbic syndrome have been reported with myoclonic movements. The syndrome is commonly due to vascular disease but it has also been described in cases of disseminated sclerosis. The onset of the abnormality is usually apoplectic but the patient seldom loses consciousness. One side of the body becomes weak. The muscles do not, in uncomplicated cases, develop the spasticity seen in hemiplegia; instead, the extremities on the abnormal side tend to remain flaccid and weak. It is commonly reported that the reflexes are brisk on both sides. There is seldom a Babinski reflex. Often abnormalities of movement are present in the affected arm and leg suggestive of those observed with cerebellar injuries. The myoclonic movements do not usually appear immediately following the vascular accident; instead, they are not observed for periods of days and weeks.

A definite system of fiber tracts is abnormal

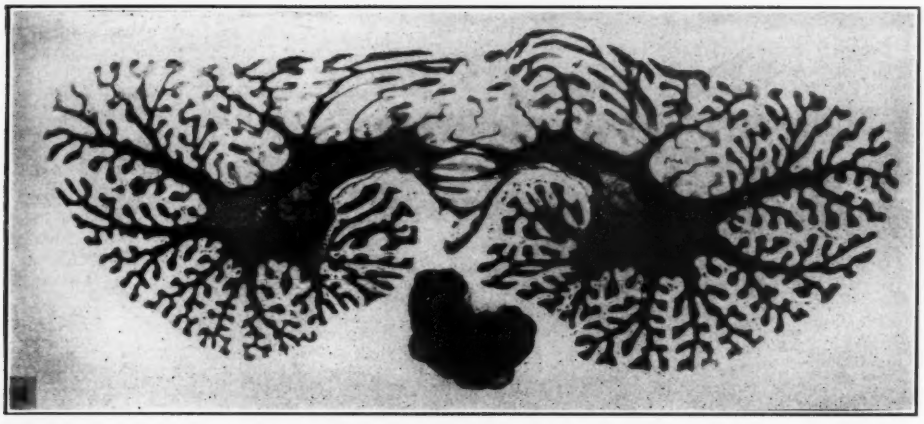

Fig. 4
"Pseudohypertrophic" degeneration in the lateral part of the right dentate nucleus. The left pyramidal tract shows some damage. At this level both olives seem normal.

Fig. 5
Section of medulla at a level somewhat craniad to that of figure 4. "Pseudohypertrophy" is seen in a portion of the left inferior olive.

in the cases of palatal myoclonus. A pathway extends downward from an unknown group of cells in the region of the thalamus or basal ganglia to end around the inferior olivary nucleus. This tract is commonly called the central tegmental fasciculus or, by Ranson, the thalamo-olivary tract. The fibers from the cells of the olive cross the midline to enter the corpus restiform of the opposite side. In this way they reach the cortex of the cerebellar hemisphere where they make connections with cells whose axones run to the dentate nucleus. The fibers from the dentate nucleus form the brachium conjunctivum, cross in the midline, and some of them terminate around the cells of the red nucleus. The fibers from these cells again cross the midline forming the rubrospinal tract. Certain of the fibers from the dentate nucleus extend upward beyond the red nucleus to the thalamus. Another neurone is thought to carry the impulses to the cerebral cortex. The myoclonus, if limited to one side, appears on the same side as the injured dentate nucleus and on the opposite side from the abnormal olivary nucleus.

The majority of the lesions producing palatal myoclonus have involved the central tegmental fasciculus. However, cases of primary damage in the inferior olivary nucleus, olivo-cerebellar fibers and dentate nucleus have been found.

The two brains described here present primary lesions of different degree. In the first one, half of the cerebellum including the dentate nucleus was destroyed, in the other there appeared to be a minute injury producing changes in only a portion of one dentate nucleus.

The first case showed well-marked changes: the inferior olive was completely degenerated. The olivo-cerebellar fibers were lost and the cerebellar peduncles on the side of the softening were totally destroyed. The capsule of the red nucleus was lost.

In the second case there was apparently only a partial degeneration producing changes in only some portions of the nuclei. Thus lesions were observed in the anterior portion of the inferior olive and the lateral portion of the dentate nucleus.

There have been several other cases reported in the literature in which the "pseudohypertrophic" degenerative changes involved only a portion of the inferior olive and dentate nucleus but no discussion of these partial lesions has been attempted. They are of considerable importance from an anatomical point of view in determining the connections and relationships between the different portions of the inferior olivary and dentate nuclei.

In the first case with degeneration of one dentate nucleus and its connections, there were bilateral myoclonic movements. In the second patient the myoclonus was predominantly, if not entirely, confined to one side and here partial destruction of one inferior olive and dentate nucleus was present. Unilateral manifestations are unusual. It is possible that they are observed only when there is a partial degeneration of one inferior olivary nucleus and its connections.

It is unusual to have degeneration extend beyond one neurone to involve other cell units in a reflex pathway. In the first and also in the second case it is possible to follow degeneration through several synaptic junctions. Thus with involvement of the dentate nucleus the degeneration extends to involve the inferior olivary nucleus. Although the axones of the olivary cells were involved in the cerebellar degeneration one would hardly expect such a marked reaction in their parent cells. The dentate nucleus gives rise to the fibers which make up the brachium conjunctivum. The loss of these fibers leads to degeneration of the capsule of red nucleus.

We must realize that the fibers of the inferior olive make only an indirect connection with the dentate cells. The olivary fibers end in the cerebellar cortex whence another intercalated neurone carries the stimuli to the dentate nucleus. The cerebellum receives many other afferent stimuli in addition to those from the inferior olivary nuclei.

It would appear from the preparations that the capsule of myelinated fibers surrounding the red nucleus is completely destroyed when the fibers of the superior cerebellar peduncle degenerate. Davison, Riley and Brock[4] pointed out that the secondary changes in the olivary cells following lesions of the central tegmental fasciculus are the result of trans-synaptic degeneration. It appears that, in cases where the lesion occurs in the central tegmental fasciculus, this form of degeneration extends over four or five neurones.

In our cases the primary injury appears to have involved the dentate nucleus of the cerebellum. Foix believed that injury of the central tegmental fasciculus and "pseudohypertrophy" of the inferior olivary nucleus were the important lesions. Guillain on the other hand contended that the essential lesion was in the olivary nucleus. Davison, Riley and Brock pointed out that the inferior olivary nucleus was implicated in all the cases of palatal myoclonus which have been reported.

The architecture of the olivary complex gives the appearance of "pseudohypertrophy" in sections prepared with myelin sheath stains because the surrounding central tegmental tract and the olivo-cerebellar fibers of the hilus are demyelinated and replaced by glial tissue, thus giving the nuclear mass a swollen and indefinite outline. Part of the enlargement of the nuclear outline is also caused by the swollen nerve cells and increase in glial cells and fibers. In the cellular stain the convolution pattern of the olive appears well preserved but somewhat thickened.

SUMMARY

The structural changes in the central nervous system of two patients who showed the palatal myoclonus syndrome are here described. One case had almost complete softening of one-half of the cerebellum with destruction of the dentate nucleus. The contralateral inferior olive showed the condition of "pseudohypertrophic" degeneration. In the other case this form of degeneration was confined to the lateral portion of one dentate nucleus and the anterior portion of the opposite inferior olivary nucleus.

These findings are similar to those described in many other patients showing palatal myoclonus. In these cases the extension of trans-synaptic degeneration is noteworthy as it involves several neurones of the inter-connected pathways.

BIBLIOGRAPHY

1. Foix, C.; Chavarny, J. A.; and Hillemand, P.: Le syndrome myoclonique de la calotte. Etude anatomo-clinique du nystagmus du voile et des myoclonies rhythmique associees, oculaires, faciales etc. Rev. Neurol., **45**:942, 1926.
2. Guillain, G.; and Thurel, R.: Myoclonies velo-pharyngo-laryngo-oculo-diaphragmatiques associees a des myoclonies synchrones squelettiques. Rev. Neurol., 2:677-684 (Dec.) 1932.
3. Guillain, G.: Syndrome of synchronous and rhythmic palato-pharyngo-laryngo-oculo-diaphragmatic myoclonous. Proc. Roy. Soc. Med., **31**:1031-1038 (July) 1938.
4. Davison, C.; Riley, H. A.; and Brock, S.: Rhythmic myoclonus of muscles of palate, larynx and other regions; histopathologic study. Bull. Neurol. Inst., New York, **5**:94-126 (Aug.) 1936.

PATHOLOGY OF KIDNEY DISEASES*

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The space allotted for this discussion is scarcely sufficient to list the pathologic changes of kidney disease. Any adequate discussion of this subject would require hours if not days of time and the manuscript of such a discussion would be a book of several hundred pages. Therefore, I shall confine my remarks to a consideration of some fundamental factors which must be taken into account in understanding the physiology and pathology of the kidney.

First let me remind you that the organ known as the kidney is a collection of separate units or organs (variously estimated at from 1,500,000 to 2,500,000) which have in common only location, source of blood supply and run-off system. Each of these units is structurally and physiologically as complete within itself and as independent of all other units as if each were in a different part of the body. Therefore the pathology of the kidney is, fundamentally, the pathology of the kidney unit or nephron and it becomes a kidney disease or mass pathology only when there is involvement of a great number of nephrons at a given time and when the pathology is the same in all nephrons involved. The pathology of single nephrons is very common, but it is not recognized clinically unless the process results in the reduction of the number of nephrons to approximately the physiologic minimum.

From the above it is evident that before we consider the pathology of the nephron, we should review those parts of the structure which are important to an understanding of the pathology and the clinical picture.

The nephron is a tubular structure composed of four histologically distinct parts: (1) the glomerulus; (2) the proximal system, including the proximal convoluted tubule and the descending arm of Henle's loop to the thin portion; (3) the thin portion of the loop; (4) the distal system, including the ascending portion of the loop and the distal convoluted tubule. The cells composing each of these four parts are so different that anyone familiar with kidney sections can tell the different parts of the nephrons in any histologic section of the kidney, yet the four parts form a continuous structure with a common lumen, and each performs a specialized function in the formation of urine.

The glomerulus is a structure of very great importance, not for the reasons usually given, but because it occupies such a key position in the blood supply of the nephron that it is all-important to the life, health, function and pathology of the rest of the nephron. But the glomerulus is not in itself necessary to urine production, as will be shown. There are persons who have functionally aglomerular kidneys, yet who produce normal urine.

The glomerulus consists of convoluted capillaries, covered by a flat epithelium (*Fig. 1*). The glomerular arteriole comes from the cortical intralobular artery. After leaving the intralobular artery there is no anastomosis with any other vessel throughout its subsequent course. The glomerular artery enters the glomerulus as the afferent artery. It divides into from three to five branches. Each branch divides usually into three branches each of which becomes a convoluted capillary which unites with other convoluted capillaries to form the efferent artery. The glomerulus, then, is composed of three to five lobes representing the primary branches of the glomerular artery, each lobe being composed of two to three lobules formed by the convoluted capillaries branching off each primary branch of the glomerular artery. There are no anastomoses between any two of these branches or between the capillaries. This is important to

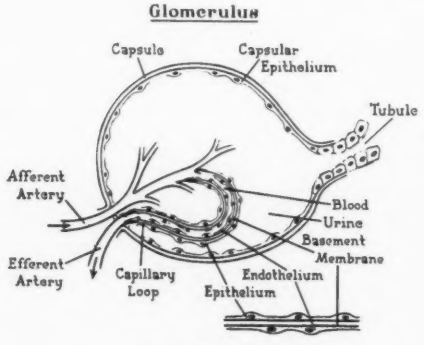

Fig. 1
Diagram showing the structure of the capillary wall in the glomerulus.

*Read in General Clinical Session, Southern Medical Association, Thirty-Second Annual Meeting, Oklahoma City, Oklahoma, November 15-18, 1938.

remember (*Figs. 2* and *3*). The efferent artery follows the tubule throughout its course and is its only blood supply. So we see that all the blood supply of the nephron passes through the glomerulus. Therefore the pathology of the glomerulus is important to normal kidney function in so far as it affects the blood supply to the tubule.

Let me illustrate. A simple form of glomerular disease is focal glomerular nephritis. There is swelling of the endothelial cells which blocks the capillary, sometimes followed by amyloid changes. The lesions are usually multiple and scattered throughout the glomerulus (*Fig. 4*). This condition becomes serious and interferes with urine production only when the lesions are numerous enough to result in a marked reduction or in complete shutting off of the blood supply to the tubule. So long as an adequate blood supply is passing through the glomerulus the tubule function will not be interfered with by the glomerular disease (*Fig. 5*).

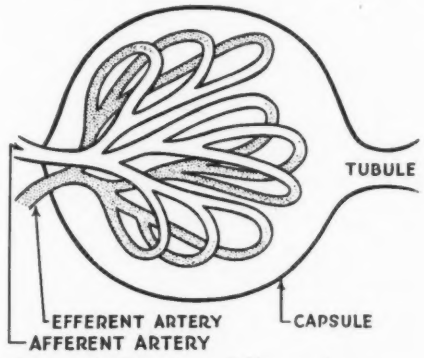

Fig. 2
Diagram to show the lobe and lobule structure of the glomerulus.

Fig. 3
Microphotograph which justifies the scheme in *Fig. 2*. Intercapillary fibrosis.

The most common of all forms of glomerular disease is capillary glomerular nephritis. In this there are an acute and a chronic phase. During the acute stage there is an engorgement of the capillaries, cloudy swelling of the epithelium and sometimes of the endothelium. As a result of the congestion and swelling of the epithelium, the glomerulus fills the entire capsule and frequently projects into the tubule. This phase is usually of short duration, lasting a few hours or a few days. During the acute phase there is an exudate from the capillaries of the glomerulus. The sequelae of this exudation are among the most important events in the entire story of nephritis.

Sometimes the exudate is washed away by the fluid escaping through the glomerular capillary walls, but more often the exudation is followed by fibrotic processes. The fibrosis may be confined to the capillary walls; it may result in obliterative adhesions between the capillary loops within the lobules (*Fig. 3*); it may in addition fuse the lobules or even the lobes into a cicatricial mass (*Fig. 6*) which may undergo hyaline degeneration (*Fig. 9-A*); there may be adhesions between the glomerular lobules and the

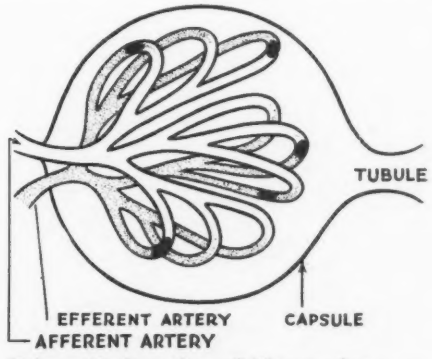

Fig. 4
Diagram of a glomerulus showing capillaries blocked in focal glomerular nephritis.

glomerular capsule (*Fig. 9-B*). Whichever one of these lesions develops, the result, so far as the glomerulus is concerned, is that the glomerulus is thereafter incapable of further function, and the nephron is thereafter an aglomerular structure (*Fig. 6*). There are many people with aglomerular kidneys who are in comparatively good health and are unaware of their condition. The most important consideration in connection with this form of glomerular disease is the effect of the end result on the blood flow through the glomerulus. It sometimes happens that one of the primary loops of the afferent artery does not take part in the formation of the glomerulus, but remains a short-cut between the afferent and efferent arteries. It sometimes happens that in spite of the fibrotic processes sufficient capillary loops persist to carry an adequate blood supply to the tubule. In either of these cases the tubule remains intact and continues to produce urine. But if the blood supply is shut off or greatly reduced the tubule atrophies and ceases to function and the functional capacity of the kidney is reduced in proportion to the number of nephrons thus lost (*Fig. 9-C*).

The pathology of the tubule is relatively simple, although it may be extensive. It consists of degeneration or necrosis due to toxic insult, or atrophy from diminished blood supply. Occasionally a tubule becomes plugged, usually by a precipitation known as a cast, in which case, due to continued function, the tubule becomes cystic. As a rule, if the patient lives, the tubule recuperates, at times regenerates following degenerative processes and even necrotic processes. An example of the latter is the bichloride kidney. Within a short time following the insult by bichloride the tubular epithelium is so necrotic that the

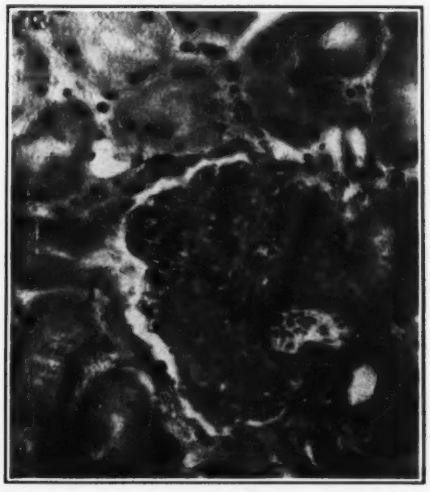

Fig. 6
Complete fibrosis of glomerulus but with sufficient blood to the nephron passing through. Aglomerular nephron.

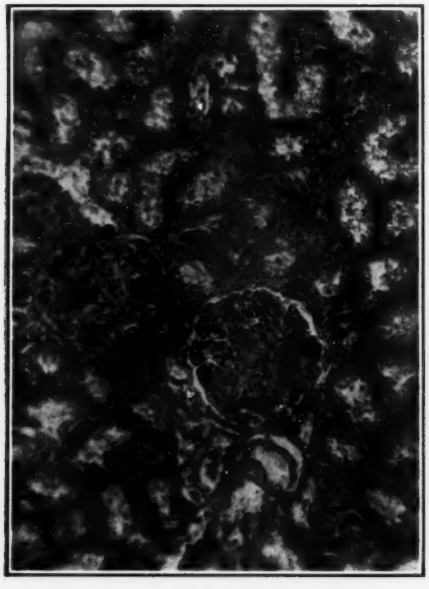

Fig. 5
Microphotograph of focal glomerular nephritis showing blocked capillaries in glomerulus.

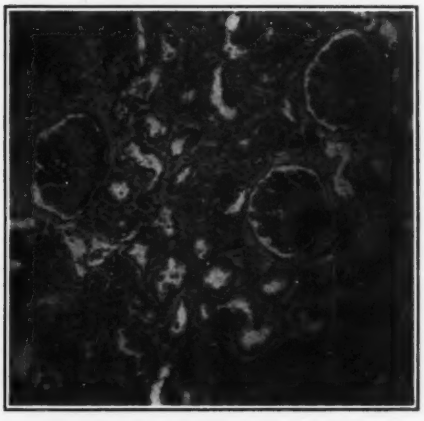

Fig. 7
Microphotograph of bichloride kidney showing regeneration of tubules. Resumption of urine production.

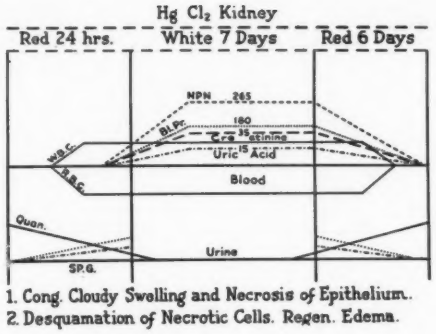

Fig. 8
Diagram showing the blood and urine picture of bichloride kidney.

kidney looks dead. The glomerulus is little if at all affected. The production of urine ceases. In about a week we find the tubules lined with a new epithelium and urine production is resumed and increases in proportion to the degree of regeneration of the epithelium (*Figs. 7* and *8*).

The regenerative power of the tubular epithelium is also shown by the compensatory hyperplasia of single tubules when the reduction in number of nephrons falls much below the normal. In cases of extreme reduction in numbers some nephrons triple their length and double their diameter so that a single nephron is capable of a function sixteen times that of a normal tubule (*Fig. 9*).

For a few minutes let us consider the so-called arteriosclerotic kidney. There is an arteriosclerotic kidney, but it is rare and does not present the picture usually known as the arteriosclerotic kidney. Because arteriosclerosis is found in a reduced kidney does not necessarily mean that the arteriosclerosis caused the reduction. It may have followed it. Arteriosclerosis always destroys the elasticity of the artery wall, hence prevents the changing blood supply required by changes in the functional demand on an organ or part. Arteriosclerosis usually reduces the carrying capacity of the vessel involved. A permanent reduction in the volume of blood always results in atrophy of the tissues supplied by the vessel involved.

There are five divisions of the afferent blood supply to the kidney parenchyma. Arteriosclerosis gives a different picture, according to which of these divisions is involved. If the lesion is in the renal artery the whole kidney atrophies. If the lesion is in a branch of the renal artery, a section of the kidney is atrophied; if in a secondary branch, a lobe is atrophied; if in the intralobular artery, lobules are atrophied; if the lesion is in the glomerular artery, the entire nephron will be atrophied. But in each case the part of the kidney involved would show uniform and symmetrical reduction. This is not the picture of the so-called arteriosclerotic kidney. It is irregularly reduced. It has a granular appearance due to small elevated light colored areas scattered over the generally depressed darker colored surface. A microscopic examination of a section of the cortex of such a kidney shows that the elevated areas are occupied by nephrons which were normal enough to carry on urine production up to the terminal events. These nephrons often show compensatory hyperplasia. The interstitial depressed areas are occupied by glomeruli showing the lesions described in the early part of this paper, and the connected tubules atrophied to mere epithelial cords with a lumen. This is not a progressive

Fig. 9
Microphotograph of cortex in chronic "interstitial arteriosclerotic" kidney. (A) Hyalinized mass representing once functioning glomerulus. (B) Completely fibrosed glomerulus with points of adhesion to capsule. (C) Region of atrophied tubules from glomeruli A and B. The remainder of the photograph, compensatory hyperplasia of nephron functioning up to time of death.

process beginning at some time and progressing to the condition seen at autopsy. It is a cumulative process. Following attacks of acute nephritis during febrile and toxic diseases some nephrons are lost by the processes described above. With each succeeding attack more nephrons are lost. The condition does not give rise to definite symptoms until the physiologic minimum is approached. The final point is that the condition is not due to arteriosclerosis, although arteriosclerosis is often a concomitant condition at autopsy and follows rather than precedes the parenchymatous changes.

In closing I wish to say that in the so-called kidney diseases, nephritis, nephrosis, and so on, the pathologic condition in the kidney is but a part of the picture and a result of a general systemic or special condition elsewhere. Just as diabetes is not a kidney disease, as it was once thought to be, so neither are nephritis nor nephrosis essentially kidney diseases. For example, albuminuria is but an evident manifestation of a general albumin loss from the capillary bed throughout the body. It is true that the effects of kidney disease are reflected in systemic symptoms, but the kidneys are not the primary culprits. As a rule if the kidneys are let alone and the outside pathologic conditions corrected, the kidneys survive and revive without special treatment.

ECTOPIC ENDOMETRIAL TISSUE OCCURRING IN CONNECTION WITH LIPOMA AND SPINA BIFIDA OCCULTA*

REPORT OF A CASE

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Miss Mary L., aged 16, was admitted to the surgical service of Anderson County Hospital on January 7, 1939, for relief of a tumor over the sacral region.

Her parents stated that the patient had had a small, soft mass over that area since early infancy. Slow increase in the size of the tumor was noted until the onset of puberty two years previously. Since that time, there has been a more rapid increase in the size of the mass. At present it caused moderate disfigurement and slight annoyance. There had been no motor or sensory disturbances of the lower extremities, and no history suggesting bladder involvement could be obtained.

The patient was somewhat underweight. The physical findings were otherwise normal with the exception of a soft, doughy, non-fluctuant tumor mass 4 x 6 inches in the midline over the lower lumbar and sacral area. The preoperative diagnosis was lipoma.

Under local anesthesia, an elliptical incision was made, beginning at the fourth lumbar vertebra and carried down to the sacrum, completely encircling the fatty tumor. Dissection of the inferior surface demonstrated a stalk projecting into the spinal canal below the fifth lumbar vertebra, the spinous process of which was found to be absent (*Fig. 1*).

Inspection of the projecting appendage demonstrated a chocolate-colored cord about 4 mm. in diameter, enveloped in a fatty capsule.

The cord and fatty covering were doubly clamped with small hemostats at the point of emergence from the spine; a catgut ligature was placed about the stump of the stalk and, after severing, it was allowed to fall back into the spinal canal. The opening due to absence of the spinous process and lamina of the fifth lumbar vertebra was closed by fascial flaps secured from along the side of the spine. The wound was closed and small rubber tissue drains emerged from each end of the incision.

The postoperative diagnosis was lipoma. (However, the specimen was sent to the pathologist with hemostats grasping the cordlike structure, which by this time had contracted almost beyond sight into the main body of the tumor. The special attention of the examiner was called to this feature and a request was made for a thorough search for nerve tissue.)

The wound healed satisfactorily and the patient was discharged from the hospital on the ninth day to finish her convalescence at home. The wound healed completely and no residual symptoms were noted.

The specimen presented for pathologic examination was wedge-shaped and measured 14 x 8 x 5 cm. The base or outer surface was covered by an elliptical section of skin and the under surface tapered down to a blunt point.

Viewing this excised mass in a casual manner, the

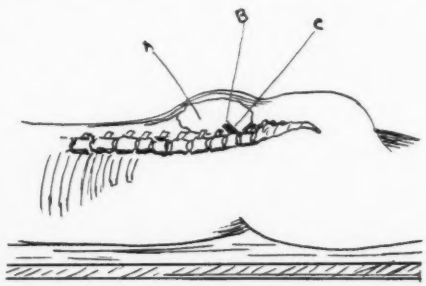

Fig. 1

Schematic presentation showing relationship of main body of tumor mass to underlying structures. (A) Lipoma, (B) Cord-like projection of endometrial tissue entering spinal cord at fifth interspace. (C) Malformation of fifth lumbar vertebra, absence of spinous process.

*Received for publication May 30, 1939.

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obvious conclusion to be reached was that the entire structure was a lipoma and that it was homogeneous. Dissection of a tail-like apendage, protruding 1.5 cm. below the under surface, revealed a dusky blue, beaded, tough, cord-like process, its diameter varying from 2 to 5 mm. (*Fig. 2*). It passed upward for a distance of 1 cm. into the main body of the neoplasm, where it terminated in connective tissue fibrils which blended into and were lost in the fatty tumor.

Sections cut from different areas of the appendage revealed, when viewed under the low power lense of the microscope, that the structure was tubular rather than solid (*Fig. 3*). The central canal was lined with columnar epithelium, some of which presented cilia and resembled cells of fallopian tube origin. An island, corresponding to about one-sixth of the area of the wall of the tubular structure, contains an array of simple glands lined by a single layer of columnar epithelium, being well spaced and separated by a loosely woven, cellular stroma. Under high power observation, both glands and stroma appear identical with that found in the normal, functioning uterine mucosa (*Fig. 4*). The remainder of the structure is composed of connective tissue and nonstriated muscle fibers, not unlike those of the uterus.

Sections cut from the main body of the tumor demonstrated a structure typically lipomatous. No nerve tissue was found.

The anatomical diagnosis was ectopic endometrium and lipoma.

Pathologist's Summary.—A specimen is reported in which definite ectopic endometrium has been encountered in connection with a lipoma overlying and penetrating a spina bifida occulta. Several theories concerning this unusual finding can be advanced. One is that it may be a vestigial remnant of the mullerian duct and the other is that it is teratomatous. The latter theory is favored by this writer, and Ewing[1] says in this connection: "The association with spina bifida throws some light on the pathogenesis of the entire group of sacral teratomas, since spina bifida signifies a lack of coherence of embryonal parts and a failure of growth momentus, which is favorable to spasmodic and aberrant growth of the type of budding."

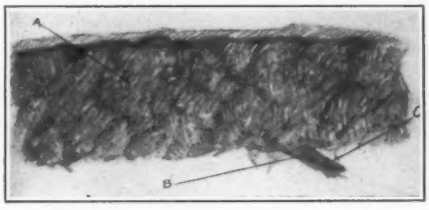

Fig. 2

Excised tumor mass. (A) Fatty structure (lipoma). (B) Envelop of fatty tissue investing cord-like process of endometrial tissue. (C) This cord-like projection composed of endometrial tissue shown in figures 3 and 4.

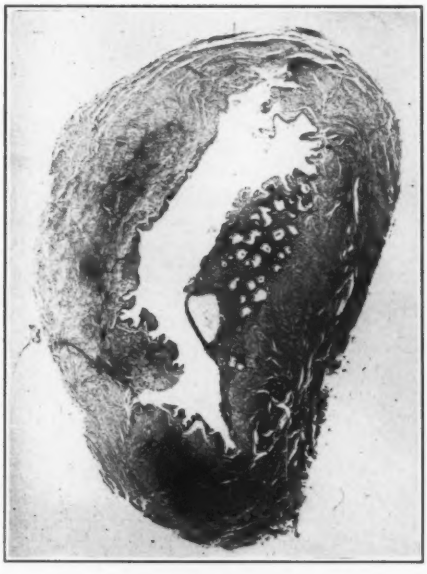

Fig. 3

Low power photomicrograph showing tube-like structure with epithelial lining. Cilia can be distinguished on some of the cells. The island of endometrium is shown together with the fibromuscular wall.

Fig. 4

High power photomicrograph showing typical endometrial arrangement of cells and stroma with underlying structures suggestive of uterine muscularis. High magnification of ribbon of lining cells is also shown. These possess cilia and are apparently of tubal origin.

1. Ewing, James: Neoplastic Diseases. Third Edition, p. 1038. Philadelphia: W. B. Saunders Co., 1931.

Upon completion of our laboratory studies of the tissue, clinical history and sections were submitted to Dr. Emil Novak for evaluation. In a communication[2] dated February 1 he says that he is in complete agreement with our interpretation of the microscopic picture. In regard to the possible source of this, Dr. Novak said that in his opinion it was undoubtedly of mullerian duct origin and not a true endometriosis. However, a pelvic examination was advised to rule out the possibility of endometrial implants in that region.

The following, concerning recommendations for subsequent management of the case, is quoted from Dr. Novak's letter:

"It would certainly seem to me to be unwise to do anything further in an effort to remove any possible endometrial tissue in the spinal column, or to subject the patient to radiation therapy of any sort in an effort to bring about retrogression of the endometrium, the latter course, for example, being attended with the danger of bringing about a premature menopause, as any dosage sufficient to insure retrogression would have to be a sterilizing dose. If the patient is in pretty good shape and has no particular symptoms, I would certainly think it best to mark time for the present, though I do believe that it would be worth-while to make a thorough examination of the pelvic organs, even if this involves a light gas anesthesia."

Examination April 19, 1939 (three and one-half months postoperatively) showed that the patient had gained eight pounds in weight and her general condition had improved to a considerable extent.

Pelvic examination under light sodium ethylthiobarbiturate anesthesia revealed a freely movable uterus of normal size, in the forward position. The adnexa were apparently normal with no suggestion of fixation or infiltration in the broad ligaments or *cul-de-sac*.

Roentgenologist's Report.—(Dr. Frank Wrenn) Stereoscopic x-ray plates taken of the spine April 19 demonstrated an elongated hiatus from the fourth lumbar vertebra through the first portion of the sacrum. The lamina of the fourth vertebra did not quite meet in the midline posteriorly to form the spinous process. This process was bifid with some separation between the prongs. The same condition, markedly exaggerated, exists in the fifth vertebra and the first portion of the sacrum.

The x-ray diagnosis is spina bifida occulta.

SUMMARY

A case is reported in which endometrial tissue was found underlying a well-defined lipoma and penetrating the spinal canal by way of a spina bifida occulta.

CONCLUSIONS

The problem faced was definitely to determine whether or not the lesion under scrutiny was an embryonic anomaly that would be permanently eliminated by excision or an atypical endometriosis, the dimensions of which would increase with each menstrual period. In the event of the latter, the question arose of the best means of eliminating the endometrial tissue remaining in the spinal canal.

In view of Dr. Novak's recommendation, no action was taken and the subsequent progress of the patient seems to contraindicate any further operative or radiologic interference.

We wish to express our sincere thanks to Lieut.-Col. J. E. Ash, Medical Corps, U. S. Army, and his associates at the Army Medical Museum for their courtesy in furnishing the photomicrographs used to illustrate this paper.

CHONDROMYXOSARCOMA AND OSTEOCHONDROSARCOMA*

By L. E. SORRELL, M.D.
Birmingham, Alabama

There is voluminous literature on the classification of bone tumors. All bone tumors are composed of connective tissue, cartilage and bone cells. The predominating tissue usually gives the pathologic diagnosis.

Geschickster and Copeland classify chondromyxosarcoma as primary and secondary.

The primary type usually occurs in patients under 30 years of age, the ages being most frequently between 12 and 21 years. The regions most commonly affected are the lower ends of the femurs, upper ends of the tibias, upper ends of the humeri and the pelvic girdle. The location of these lesions has a definite relation to muscular insertion and tractions, especially the long muscles. There is also a definite relation at these points in the fibrous tissue, periosteum and cartilaginous tissue.

The patient usually presents himself four or five months after the first symptoms have been noticed. Pain is the first symptom in most cases and may or may not be associated with trauma. If the lesion is at the knee the patient as a rule complains of pain and stiffness, and the knee, as a rule is partially flexed, walking is painful and the patient may have to use crutches. Relief may become impossible when the patient is at rest, without sedatives.

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*Read in Section on Radiology, Southern Medical Association, Thirty-Second Annual Meeting, Oklahoma City, Oklahoma, November 15-18, 1938.

Examination of the region at this time will reveal a flexed knee joint with a hard tumefaction almost the consistency of bone, the tumor mass appearing larger than the x-ray films would seem to indicate. The patient usually has fever, leukocytosis and occasionally the regional lymph nodes may be enlarged. However this is rare.

Roentgenographic Manifestations.—In primary chondrosarcomas there are three important features. The tumor as a rule does not involve the cortex or the medulla of the bone when first seen. There is a soft shadow next to the bone and the periosteum and a tumor mass appear to be raised slightly. In early cases the entire tumor is outside the bone and it may be overlooked or wrongly diagnosed. Later when calcification occurs there may be fine radiating lines at right angles to the cortex. As the tumor advances the cortex and medulla are destroyed and there may be pathologic fractures.

Gross Pathology.—A biopsy reveals a raised perforated periosteum, pearly gray with a shiny substance of variable consistency which is well formed cartilage, cystic and hemorrhagic. The lobules that form the tumor have a tendency to extend up and down the bone and around it rather than to invade the marrow cavity. In advanced cases the cortex has been broken through and the medulla has been invaded.

The microscopic study of primary chondrosarcomas will show the entire embryology of bone. One can see the early stages of cartilage formation from connective tissue, as well as the advanced calcifying forms. The substitution of cartilage by bone may be seen in this picture when one studies the histogenesis of this type of tumor and it is evident that this type of sarcoma has a definite relation to the primitive precartilaginous type. This is proven by the development at the sites where the tendons attach to the bones and by the progressive stages from connective tissue to cartilage, to bone.

Prognosis and Treatment.—The location of the tumor and the duration at the first examination bear a definite relation to the prognosis and cure. Amputation is a treatment of choice and Geschickster and Copeland report 12 per cent cures. The prognosis as a rule is worse for children than adolescents and the entire clinical course is about 18 months to 2 years. Radiation does not seem to change the course of the disease.

Secondary Chondromyxosarcoma. — These tumors occur in patients over 30 years of age, whereas the primary type occurs in patients between the ages of 12 and 21. The secondary type usually occurs on benign osteochondroma. The location of these tumors differs from that of the primary tumors, in that they occur more centrally in the bone. The most common locations are near the upper end of the humerus and in the ribs. The rate of growth is much slower than the primary tumors and the clinical course of the disease is three to four times longer. There may or may not be a history of trauma and the growth may be treated several years previously as an injury. The mass may later spring into prominence suddenly causing pain and swelling. The pain and swelling may be suspected as a rheumatic condition and if near a joint it may cause flexion. This tumor usually rises from an osteochondroma on one of the larger bones. This can usually be confirmed by a careful history. There may be a history of previous injury and swelling and persistent soreness at the point for years with an apparent cure of the injury. Several years later following the injury with or without cause, pain, swelling and pressure symptoms may cause the patient to consult a physician. If a patient presents himself complaining of a rheumatic type of pain over a period of several years and an enlarged growth, it is well to suspect a secondary chondrosarcoma. Pathologic fracture is rare in this type of tumor.

Roentogenographic Features.—The most easily recognized secondary chondrosarcomas are the ones seen arising from a primary osteochondroma. It is recognized as having a fuzzy appearance superimposed on a benign bone base. If the disease advances the tumor mass becomes a part of a granular infiltrating tumor and it invades the cortex and medulla. Before the process reaches the medulla the differential diagnosis may be extremely difficult from osteochondroma, sclerosing osteogenic sarcoma, and myositis ossificans. The differential diagnosis between this type of chondrosarcoma and an exostosis and the benign type of bone tumor is very difficult in some cases. In traumatic myositis ossificans in which the duration is short and the ossification is well defined and stationary the diagnosis is not difficult, but when the myositis ossificans is progressing and the lesion is shaggy it is difficult to tell whether the growth is benign or secondary chondrosarcoma. Biopsy is the only way to make a positive diagnosis. Sclerosing osteogenic sarcoma has greater density of the

periosteum than secondary chondrosarcoma and it scleroses the marrow cavity rather than destroying the cancellous bone. It is difficult pathologically in secondary chondrosarcoma to differentiate osteochondromas from chondromyxosarcomas. The crux is that one must differentiate benign osteochondroma from secondary chondrosarcoma and primary chondrosarcomas. In some cases it is very difficult to distinguish between the lesions under the microscope.

When the diagnosis of secondary chondrosarcoma is made the patient will live two or three years and in some cases longer. The tumor grows much more slowly than in the primary type. The percentage of cures in secondary chondrosarcoma is better than in primary chondrosarcomas. This may be due to the age of the patient and the slow growth of the tumor. Patients with secondary chondrosarcomas as a rule are over 25 years of age and the tumor grows slowly.

I wish to report two patients with primary chondrosarcomas:

Case 1.—A. G., a white boy, age 16, an American of Italian extraction, had an irrelevant family and past history. No history of trauma was obtained. He was admitted to the Norwood Clinic March 8, 1933. His chief complaint was pain and swelling of the left knee, of about 4 months duration. He came in with a diagnosis of rheumatism. On examination his left knee was seen to be flexed and it was about 50 per cent larger than the right with a firm tumefaction. The knee was warm to touch, and it was quite painful. His temperature ranged from 99 to 102.° Urine examination was negative. He had 6 per cent eosinophils and 12,800 white blood cells, otherwise the blood was within normal limits. Radiologic examination of the knee at this time revealed an increased infiltration of the soft tissue on the inner side of the lower third of the thigh with slight elevation of the periosteum at one point with no cortex destruction. A diagnosis of sarcoma was made. The patient refused amputation. He left the hospital and returned about 10 days later. The x-ray examination on that date revealed considerable progress of the disease in the soft tissue and some cortex destruction. Amputation was done in the upper third of the thigh. Recurrence in the stump occurred in about two months and metastases in the inguinal glands. Metastases developed in the chest four months after operation and he died five months after operation.

Microscopic Description.—The tumor consisted largely of atypical cartilage cells of varying size and irregularly arranged. Some cells were of giant size and there were many mitoses. There were occasional traces of calcification and a few bone trabeculae which were suggestive of new forming bone.

The diagnosis was chondrosarcoma.

Case 2.—L. H., a white man, age 20, was admitted to the Norwood Clinic December 4, 1934 complaining of pain and infection of the right knee of two months' duration. There was a draining sinus just below the knee on the anterior surface of the leg. The knee was flexed, painful, warm to touch and there was a tumefaction in the upper third of the leg about twice the size of the opposite leg. His temperature was 100.° Blood and urine were normal. Family and past history are irrelevant and no history of trauma was obtained. This patient came to the clinic with a diagnosis of osteomyelitis or abscess. Radiologic examination on December 4, 1934, revealed some destruction of the bone cortex of the anterior upper third of the tibia. The periosteum adjacent to the area below this was slightly elevated, with a tumor mass in the soft tissue. A diagnosis of chondrosarcoma was made. The patient refused amputation, left the hospital and returned 18 days later, and radiologic examination at this date revealed considerable destruction of the cortex and discreet areas of calcification throughout the tumor mass. Amputation was done in the upper third of the thigh at this time and the patient died five months later with metastases of the lungs.

Microscopic Report.—Section showed a tumor with a regular column of immature cartilage cells some of which contained a central trace of necrotic calcified cartilage. Most of the tumor, however, consisted of loosely arranged large cells which often outlined the spaces with blood and sometimes were lined by epithelium and at other times by a tumor cell. The tumor cells were varied in size and large numbers of them were giant cells of multiple nuclei. Mitosis was frequent and sometimes multipolar.

The diagnosis was chondrosarcoma.

COMMENT

Two patients with a positive diagnosis of chondrosarcoma with lesions near the knee have been described, both of whom might have been saved had they been seen and diagnosed when the symptoms first began. The first patient refused amputation on first examination and later had drainage tubes inserted when a mistaken diagnosis of osteomyelitis was made. The lesion of the second patient was incised before he was first seen. The diagnosis had been previously made as an abscess. He had been given salicylates and typhoid vaccine for a rheumatic knee.

If we can impress the general practitioner, who sees most of these patients first, with the fact that an enlargement or painful growth any where on the body is a dangerous symptom and the patient should receive an immediate diagnosis and treatment, the mortality rate in these cases can be lowered.

DISCUSSION (*Abstract*)

Dr. Alfred J. Ackermann, Oklahoma City, Okla.—The subdivision of osteogenic sarcoma in various groups presents great difficulties to the pathologist, and more to the roentgenologist.

From a practical standpoint, such a classification is justified whenever certain characteristic features of the tumor influence their clinical course and final prognosis, which considers the type of treatment now available.

The differentiation of bone tumors on the basis of their cellular characteristics alone is inaccurate, because such names do not convey sufficient data of diagnostic importance.

The majority of tumors among osteogenic sarcomas contain cartilage in association with a type of myxomatous connective tissue, indicating an origin analogous to the benign exostoses and chondromas.

Roentgenologically the various types of osteogenic sarcoma are insufficiently distinct to permit a differential diagnosis. The localization, extent of bone involvement, soft tissue swelling, and bone spicules, or calcifications within the soft tissue, vary so greatly in the same type of tumor that when advanced these changes cannot be utilized in differential diagnosis.

The reaction of the periosteum is not pathognomonic of any of these tumors. Undoubtedly there may be some variations, not sufficient, however, to be depended upon.

Calcification within the soft tissues occurs, not only in osteogenic tumors, but it is found quite frequently in fibrosarcomas. Calcifications within hematomas, due to myositis ossificans, have been mentioned by the author.

Less difficulty is encountered in secondary chondrosarcomas, which show malignant changes within a primarily benign tumor.

In summary, we feel that the classification accepted by the Bone Registry Committee, serves the general purposes, without causing confusion, which is especially great in the field of the pathology of bone tumors.

Dr. L. S. McAlister, Muskogee, Okla.—I have been looking over Dr. Sorrell's paper for a week or ten days now and I wish to praise his practical way of disposing of the pathologic classification. I have also just finished reading Kolodny's classic on bone sarcoma, but I feel that Dr. Sorrell's paper has given me a practical conception of the subject which I was unable to derive from the former. The spirit of optimism with which he closes should also be praised, for without it a physician is as welcome among the victims of malignancy as an undertaker.

For this reason I should like to urge that the therapy rooms of all radiologists be made as light and cheerful as possible and that the interiors be white instead of a cold gray lead an eighth of an inch thick.

My first encounter with a bone tumor was during my senior year's medical work, when I saw a Ewing's tumor in an infant. It received moderate voltage therapy and died a little later. During my internship I did not see a bone sarcoma, but one of the staff physicians had just recently taken care of one which died. During the eight years I have just spent in private practice of radiotherapeutics I have seen one Ewing's tumor of the femur of an eighteen-year-old daughter of a Christian Scientist. The tumor was treated for a few days by moderate voltage therapy when the parents decided to use faith instead. The patient died.

Two years ago I saw a woman of seventy with a red, tender swelling on the sole of one foot of about one month's duration. (The case was analogous to a subfascial abscess I had seen a few weeks before, which healed following incision and drainage.) The elderly lady's roentgenogram showed no bony change suggestive of sarcoma, but it did show a bulging plantar fascia. This was incised but no pus was found. Death followed shortly after amputation by a competent man. X-ray therapy was offered before and after, but was refused. This case, although of no credit to me, is mentioned to illustrate the value of a careful history when the case is first seen. To be sure, the red tender swelling was only three or four weeks old, but I failed to elicit the fact that she had also had slight pain in the foot for about one year prior to the acute pain. In retrospect, I can make the diagnosis of extraperiosteal fibrosarcoma.

I have had no personal experience with the treatment of bone sarcoma at two hundred kilovolts as I have had such equipment available for only a year and during this time have seen no suspicious looking bone tumors.

From the literature and various books, I have formed the opinion that destructive doses of irradiation followed by amputation might be successful, especially in bones of the distal extremities.

I recently looked through a file of radiographs of bone sarcoma at the University of Nebraska through the courtesy of Dr. Howard Hunt. The percentage of pulmonary metastases was extremely high, but in spite of the disheartening mortality, we must keep trying.

RECENT PSYCHOLOGICAL APPROACHES TO PATIENTS WITH ALCOHOL PROBLEMS*

By ROBERT V. SELIGER, M.D.†
Baltimore, Maryland

Society has termed individuals with alcohol problems alcoholics and chronic alcoholics. The terms alcoholic and chronic alcoholic as used here include only the pathologic drinker and definitely exclude the social drinker. The social drinker can "handle" his or her alcohol, while the other is "handled" by alcohol. That is, social drinking does not interfere with the individual's important life activities in business, in the home, in the family and in the community. Problem drinkers, uncontrolled drinkers, dipsomaniacs and spree drinkers are all pathologic drinkers. Chronic alcoholism is a very complex social and medical problem. I do not feel that all chronic alcoholics necessarily are poorly integrated individuals. Henderson and Gillespie say:

"Chronic alcoholism develops in a wide variety of

*Read in Section on Neurology and Psychiatry, Southern Medical Association, Thirty-Second Annual Meeting, Oklahoma City, Oklahoma, November 15-18, 1938.

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persons; in some because of opportunity (barmen)—in others because of the social environment, and in others it begins as a reaction to difficulties or as an expression of a psychopathic disposition (manic-depressive, for example)." The vastness of the whole problem is brought out by Forel, who says: 'In all countries where alcoholism reigns, it accounts for from one-half to three-fourths of the crimes, a great share of suicides, of mental disorders, of death, of diseases generally, of poverty, of vulgar depravity, of sexual excesses and venereal disease and of dissolution of families. The worst feature is the production of deformed progeny by direct degeneration of the tissues.'"

Successful results measured by total abstinence have been obtained by many approaches both lay and medical. Occasionally chronic alcoholics have rehabilitated themselves, others have been helped by friends, some by religious conversion, and others by temperance pledges. In Switzerland remarkable results have been obtained by a more or less lay society, "The Blue Cross." According to Henderson and Gillespie, "Psychological treatment has proven of great value in isolated cases more often than is generally realized." In a previous paper the author stated that although many alcoholics were past correction, certain selected patients could be helped and guided to the goal of therapy, total abstinence.

VARIOUS APPROACHES TO THE PROBLEM

One finds that in recent years many persons have obtained very successful results with individual forms of therapy or rehabilitation, some of which are given below:

Forel repeatedly, at the Brussels, Brenan and Hague Congresses, maintained that the only efficacious method of treatment of chronic alcoholism and dipsomania was complete and permanent abstention from all fermented and distilled drinks. He had never found that sudden and entire suppression of alcoholic drinks in such cases had any injurious effects. He relates that when he first began to treat alcoholic patients without alcohol people laughed at him and said that his patients would die like flies. Their gloomy predictions, however, were not realized, as was shown by the fact that of 500 alcoholic patients treated at the Ellikon Inebriate Home during the period 1888-97 who had been suddenly deprived of alcohol, only one case proved fatal, the patient being a tuberculous subject who was admitted in a moribund condition. Moreover, the death rate among the alcoholics at the Burgholzli Asylum during the period 1879-86, when alcohol was given, was higher than in the period 1886-97, when it was suddenly suppressed. Next in importance to complete abstention from alcohol, Forel regarded isolation for a considerable time, at least six months, in a special home under adequate supervision, where the treatment was all the more likely to be successful if the superintendent of the home was himself entirely abstinent as well as all the other inmates. After leaving the home, a system of correspondence and visits should be arranged and the patient should be induced to join an abstinence society. Hypnotism he considered to be an excellent adjuvant in obtaining total abstinence, but he declared that it was an absolutely idiotic and harmful undertaking to try to convert "a soaker" into a moderate drinker, as Hirt advised. In the great majority of such cases relapses occurred sooner or later.

Henderson and Gillespie, in discussing the treatment of alcoholism, say:

"The kind of treatment to be adopted, and the hope entertained for it, depend partly on the type of chronic alcoholic with whom one is dealing, and partly on the stage at which he comes (or is brought) for treatment. Careful investigation from a physical and a psychiatric viewpoint is an essential preliminary. Where alcohol is found to be a symptom of some disease, mental or physical, as general paralysis or a recurrent manic-depressive psychosis, the treatment is that of the underlying disease. When the alcoholic habit itself is in the forefront, the chief line of attack is a thorough investigation of the factors of the patient's life and personality. Usually the first step that should be insisted on is that the patient should place himself in a nursing home or in a hospital where he can be adequately supervised. This, of course, is usually what the patient refuses to do, but with the exercise of tact and patience it is often possible in the early stages to get the patient's cooperation. In our experience, the psychological viewpoint is usually a revelation to the patient, and the physician who places it before him is at once at an advantage; for always the patient has been taught by his friends that his condition is simply one of moral turpitude, and nearly always he has personally come to regard his alcoholism as mysterious and inevitable. The patient's good will having been gradually obtained in this way, it is usually possible to show him the factors, psychological and circumstantial, which have contributed to his illness, and to show him how they can be more satisfactorily dealt with. Advice also about the conduct of his life in future gives the patient back some of his self-confidence, which in the early stages of alcoholism has often been lost. Complete abstinence should be insisted on. The patient has usually to be taught that it is not unmanly to be abstinent. An avoidance of unnecessary opportunity for drinking is extremely important; for example, it is nearly hopeless to send him back to work as a bartender or an exciseman. The cultivation of hobbies and social recreation of a healthy kind, to replace the discarded alcoholism, is also important. When the immediate treatment is finished with, and the patient returns to work, he should be encouraged to keep in touch with his medical adviser for a year or two."

Diethelm, in discussing the treatment of alcoholism, says:

"The treatment of chronic alcoholism has usually been directed along three lines: that of personality analysis, in an endeavor to find strivings which drove the patient into alcoholism; re-education under enforced abstinence; and the use of drugs to change hypothetical chemical processes in the body or to produce a lasting disgust to alcohol through chemical alterations. The attempt to treat with drugs can hardly be called scientific and is, therefore, usually administered by non-physicians. The large number of persons who seek help in such insti-

tutions is an indi ation of the failure of medical science to outline well-planned treatment.

"The only treatment which can be effective in all cases and which can be adjusted to the patient's individual needs is treatment which combines personality analysis and adjustment with training of healthier habits over a long period of time and under strict abstinence.

"The treatment can be divided into two phases. It should begin with immediate withdrawal from alcohol and be carried out under complete abstinence. Immediate withdrawal is psychologically important. It proves to the patient that there is no medical necessity for the use of alcohol in his case, and this realization is the beginning of his re-education. The patient must break away from many of the ideas, attitudes and habits of his past life and learn that alcoholic drinks are not necessary for him to be cheerful and happy; that although they may help temporarily, in reality they increase his difficulties. * * *

"During the second phase of treatment, which deals primarily with re-education of his habits, our knowledge of his personality should permit us to utilize an individualized approach. It is desirable that this be carried out in an open institution in which the patient can lead a healthy life, with a well balanced routine which includes work and suitable recreation and a healthy physical regime."

According to Strecker and Chambers (as reviewed by Walls):

"In the treatment of alcoholism, a high goal is set: the authors believe that the successful therapist should have an absolute conviction that he can bring about such a state of mind in his patients that they will never desire to drink again. Response to treatment is defined as a climbing to higher and more mature emotional levels. At the very outset the authors' answer to the question, 'Can I learn to drink in moderation?' is emphatically, 'No.' Here they are in agreement with all sound students in this field of work. The majority of patients should have at least a month away from their usual environment. The protection of a hospital during the early stages of the treatment is not compulsory, and patients are given an opportunity to attempt the treatment without hospitalization. The family's point of view is given careful consideration. The attitude of a family long exposed to the trials of living with an alcoholic must be modified, if the best results are to be secured.

"In the first interview, it should be ascertained whether or not the individual looks upon himself as an alcoholic. The patient is given some idea of the physical effects and dangers of alcohol, and is asked to undertake a personal study of himself, combined with suggested readings. Relaxation finds a place in this type of therapy.

"The writers describe the method by which a psychologically curative conditioned reflex is established. They recommend approximately one hundred hours over a period of a year. The first three months of treatment should comprise three appointments a week, after which, if progress is favorable, the appointments may be decreased to two a week. Formulae in the form of suggestion therapy are described and vocational readjustment is recommended in certain instance. 'Obviously, the broker's office is not the place for a highly introverted personality with literary ability, nor is the stock exchange a good field of endeavor for a man whose readjustment will depend much upon his ability to face reality in all its phases.' Patients are cautioned against becoming overfatigued. The points of treatment and re-education are summarized in a useful fashion for the reader."

According to Durfee (as reviewed by Walls):

"A farm near a village is the setting in which the accepted candidate undertakes his re-education. The example and leadership of the older patients are the only means of restriction. The occupational and physical activities are carried on informally, digging in the earth having a most popular appeal. The gradual withdrawal of alcohol is stressed. In mental hospitals, psychiatrists rarely see a problem-drinker who asks for alcohol, and in the majority of cases the alcohol is withdrawn immediately without ill effects.

"The re-education program consists of a physical and mental upbuilding. Conflicts are talked over, advantage being taken of the spontaneous unburdenings at work, at play, or in interviews. Of what is accomplished the author writes: 'It is rebirth in the sense of a fresh start. The value of therapy lies in its inner power to open the way to a continuing growth. When therapy ends, that growth is just beginning.' Complete abstinence is the rule."

AUTHOR'S TREATMENT

Treatment should begin with the immediate withdrawal of alcohol. The patient should be instantly informed that the goal is total abstinence and all concerned must recognize that an individual who has been a pathological drinker can never be a social drinker. A person who has once been an excessive drinker can never be a moderate, controlled, or a one-or-two cocktail drinker. He must understand that there is a sacrifice of both time and money involved in the treatment and that the road to the goal is a long and hard one, requiring patience, determination and absolute honesty of relationship between patient and physician. He is given to understand that failures in the past under other types of treatment mean nothing and are not obstacles to his attaining the goal, and that "once an alcoholic, always an alcoholic" is a general misstatement. For months, in some patients, the only headway made is the teaching of the fact that he can live without alcohol and this realization plays a great part in his re-education.

The patient reports to the psychiatrist's office at regular intervals, at first daily or three times a week and then less frequently.

He must be punctual, in spite of inclement weather, "previous engagements" or any other issues used so often for cancellations and postponements. Coming is *his job!*

Should he feel after a few weeks of abstinence that he can go along on his own and stop coming for his interviews, the physician will not call him or otherwise remind him of his negligence. The responsibility is *his*.

He must never test himself out to determine whether or not he has the problem "beat" by taking one drink. All drinking must be stopped instantly, without any tapering off.

When a large alcohol intake is abruptly stopped, sedatives are often necessary for a while to relieve the "shakes" and any jittery feeling which may follow the withdrawal. With this the sugar intake is definitely increased and the patient is also advised to take heavy doses of vitamin B.

Psychotherapy is continued throughout interviews. Other methods of handling the need for escape from situations are considered. Very frequently it is possible to modify poor vocational adjustment, or irritating marital situations involving sexual incompatibilities, unwholesome living conditions with in-laws in the family life, parental conflict over the management of children, and so on. The patient himself may not be conscious of the strains that all these things are upon him. When it is not possible to modify the situation, it is often possible to change the patient's attitude toward the difficulties he has to meet. Many a person becomes morbidly self-accusatory and fatalistic because of what he considers his failure to modify the unmodifiable. Such an individual may be greatly helped by mutual discussions, constructive criticism and wise guidance.

The interviews are further used to outline a recreational program and develop interest in new hobbies, diversions or club activities. It is wise to have the patient at the beginning of the treatment give up his drinking friends and meeting places and replace them by nondrinking contacts. Later on he is allowed to visit friends and go to dinners where cocktails are served.

During all this time stress is laid upon the point that total abstinence is the only possible road to, and goal of, therapy.

The mate of the patient is interviewed many times, for the attitude toward drinking of wife or husband is extremely important. Their tact and diplomacy in handling past and present situations and episodes together with their intelligent cooperation in the planning of new activities are major therapeutic aids. One cannot stress too much the significance of the mate's attitude and cooperation. Many a poor result of treatment is due to the absence of any insight whatever in wife or husband.

During the early months of treatment the patient uses as a splint the physician rather than the alcohol which he has previously utilized. Throughout the treatment there is established a close personal relationship between the patient and the doctor. In this way the latter develops a definite knowledge of how the patient "ticks" and the patient derives confidence and helpfulness in realizing the physician's understanding of his own particular problems.

The patient who comes with an honest desire for help should be approached with sympathy and kindness that eliminates ideas of punishment, fears of failure and attitudes of inferiority. Patient and physician should meet each other halfway with frankness and mutual expectation of confidence. The psychiatrist's tact and diplomacy in presenting to the patient the liabilities of his make-up is extremely important.

The interviews are used for many purposes, although one cannot put in words exactly what takes place during an interview. Aside from the above psychotherapy and obtaining all the available information necessary to complete the survey of the individual, the patient is indirectly forming new habits and breaking down old ones. The interviews are also used for the permanent development of proper attitude and the patient learns to be guided by his judgment rather than his emotions. With many patients the interviews are used to discuss the individual alcohol sensitivity. A great deal of the time is also spent on individual personality disciplining. The thought processes preceding the last alcoholic bout and other bouts are gone into also. While directing the attitude of the patient to the fact that total abstinence for life is the goal of therapy, therapy should indirectly divert the mind of the patient from the whole subject of drinking.

SUMMARY

It is evident that all the above psychological approaches, that of the author as well as of several quoted authorities, have in common the following important fundamentals: that successful psychological treatment revolves around two

principles, attitude and habit formation, without which it is impossible to achieve success.

DISCUSSION (*Abstract*)

Dr. Arthur J. Schwenkenberg, Dallas, Texas.—My own experiences with this problem do not vary a great deal from those brought out by Dr. Seliger. One of the outstanding difficulties lies in the fact that pathologic alcoholism is not generally considered to be a mental illness, but rather a lack of will power. Furthermore, the fact that the laity is constantly being exploited by so-called "cures" offered by commercial institutions, and the fact that physicians and even some psychiatrists fail to regard the problem seriously from the psyciatric point of view, makes it a difficult one to attack.

I can do very little in a community like Dallas, presenting the type of alcoholic states with which I come into contact, unless the patients are placed in a controlled environment, especially a rest home type of sanitarium. Even then, I find it difficult to keep these patients in the sanitarium long enough to do much more than to assist them physically. In spite of all my efforts, the majority of my patients will leave the sanitarium as soon as they feel better, because they think they cannot spare the time from their business for further treatment, as most of them, because of their alcoholism, have gotten into debt and other difficulties.

I believe in the rapid withdrawal of alcohol. I had occasion for a period of five years to observe alcoholic patients placed in the psychopathic ward of the county jail under lunacy charges. These patients knew that no alcohol would be supplied them and after a period of some 48 to 72 hours were ready to be discharged, practically free from withdrawal symptoms. Many, because of the "lunacy charge," could be confined for a week or ten days, and these, in spite of the fact that they had been confined in jail, were very much gratified by their improvement. Although a fair per cent returned after a short interval, the majority made a better adjustment than patients who had been confined for similar periods of time in a hospital or sanitarium, especially where alcohol had been withdrawn gradually.

Not more than 5 per cent of the alcoholics who consult me do so voluntarily. Certainly, those who submit voluntarily do benefit by the approach as emphasized by Dr. Seliger.

There is still great need for psychiatric education through mental hygiene and for scientific education on the alcoholic problem. In the State of Texas it is very difficult to convict a patient under the inebriate act and even more difficult under a charge of lunacy.

For a long time I have felt that a state alcoholic farm, controlled by the proper legal statutes, would hold out hope for many of these maladjusted personalities. However, such institutions are far in the future, in spite of the fairly rapid progress which mental hygiene is making in Texas.

I am also convinced that many younger individuals, especially men, who die quite suddenly and whose death is reported to be due to heart disease, die either directly or indirectly from alcoholism.

Dr. G. Wilse Robinson, Jr., Kansas City, Mo.—One element in these cases I consider quite important in its interpretation. I do not care to express myself as to whether the change is psychologic, physiologic or biochemical, but I have seen it in almost all of my patients. Something happens which lowers the alcoholic's tolerance to alcohol. These men for a period are able to take large quantities of alcohol and control themselves moderately well, although, of course, they become intoxicated. Then there seems to come a time when one or two or three highballs or cocktails produce a tremendous personality effect, and these men, as they express it themselves, get terribly drunk on a surprisingly small amount of alcohol.

I have often wondered if this phenomenon, leading to very early and very severe intoxication which completely wipes out all sense of responsibility, is not, after all, one of the secrets of the alcoholic problem which must be solved if we are properly and completely to treat the alcoholic and his reactions to alcohol.

Dr. James Asa Willie, Oklahoma City, Okla.—Dr. Seliger distinguishes between what he calls the "pathologic drinker" and the "social drinker." To my mind this separation is convenient, but I doubt that one can always draw such a line of distinction because in many of our "social drinkers" the drinking is a symptom of illness. I certainly agree with Dr. Seliger that in the handling of the alcoholic one must be quite individualistic. One must study him as an individual and not as an alcoholic. It is important, as Dr. Seliger points out, first to make a thorough investigation. Such an investigation should include the taking of the family background, the past development, the personality study, the development of the problems presented; next, a thorough physical and neurologic examination and finally, a formal mental status.

Dr. Seliger next divides his cases into three groups on the basis of the strength of their desire to abstain, the level of intelligence and the amount of maturity of the make-up. This classification is quite useful. One group can be treated in the office, another group requires temporary institutionalization and still another group needs a more prolonged stay in an institution. Then Dr. Seliger summarizes the different recent psychologic approaches for us. The very multiplicity of approaches to the problem which the alcoholic presents and the fact that success and failure have followed the application of many different approaches should make us all the more wary when it comes to depending upon any one resource in our treatment armamentarium. In fact, I am certain that all of us have seen alcoholics who, despite the most thorough investigation, study and treatment, remain pretty much the same. This lack of response brings up the constitutional barrier which our keenest weapons of treatment have so far failed to penetrate.

I am sorry that Dr. Seliger did not tell us a little more about the psychoanalytical approach to the problem of alcoholism.

THE USE OF CRYSTALLINE ZINC INSULIN IN THE TREATMENT OF DIABETES MELLITUS*

By ROBERT C. LOWE, M.D.
LANG F. HOLLAND, M.D.
and
J. O. WEILBAECHER, JR., M.D.
New Orleans, Louisiana

During recent years extensive studies have been carried on dealing with the treatment of diabetes mellitus with various modified insulins. In this country protamine zinc insulin has been more widely used, either alone or in combination, than any other of the new preparations, and has proven to be a valuable addition to the therapy of diabetes. On the other hand, it by no means answers the needs of all patients. Our own experience has been that in certain adult cases of more than usual severity it is not effective alone,[1] and a survey of the literature seems to indicate that it has not been entirely successful in severe adult and juvenile diabetes.[2 3] In many of the reported cases a combination of protamine zinc insulin and regular insulin has proven of value, but such combined therapy lacks the simplicity which, among other desiderata, has been the aim of all research in this field.

In addition to being without deleterious effects, the ideal insulin preparation would be such that a single daily injection would adapt itself to the 24-hour cycle of carbohydrate metabolism. In spite of some evidence to the contrary,[4] it is generally agreed that its action should be most intense during the period of carbohydrate metabolism and storage, but also should be sufficient to maintain equilibrium of carbohydrate and fat metabolism during the remainder of the 24 hours.

Crystalline zinc insulin, another modification of insulin extracts, has had much less attention than it deserves. It is a crystallized insulin which was developed commercially by Sahyun in 1934.[5] Its assay, 25 to 25.5 units per milligram, compares favorably with the original preparation of Abel, which assayed 24 units per milligram.[6] Its effectiveness for routine use, as well as in diabetes with complications, has been demonstrated by Freund and Adler,[7] Mains and McMullen,[8] Altshuler,[9] Altshuler and Leiser,[10] Barach,[11 12] and Shepardson and Friedlander.[13]

Using the rate of fall of fasting blood sugar levels as a criterion,[7] it has been shown that the average duration of the action of crystalline zinc insulin is 8 or 9 hours, which is longer than that of regular insulin, although less than that of protamine zinc insulin.[7] Some effect on the level of the fasting blood sugar is still evident 24 hours after a morning dose has been given.[8]

The intensity of the action of any insulin preparation for any unit of time may be said to be roughly inversely proportional to the duration of its action if due allowance is made for a rapid or gradual decrease of insulin action paralleling the decrease of insulin content in the depot in the tissues. In this respect crystalline zinc insulin occupies a place intermediate between regular insulin and protamine zinc insulin. The intensity of its action for a given unit of time is less than that of regular insulin, but the duration of the action is longer. In comparison with protamine zinc insulin, however, the intensity of its action for a given unit of time is greater, but the duration of its effect is shorter.

Such theoretical considerations led us to believe that an insulin with the characteristics which crystalline zinc insulin had been shown to possess might approach more closely to the ideal insulin than any preparation now available. We therefore employed it in a group of patients who had proven refractive to either regular insulin and/or to protamine zinc insulin used alone or used in combination. The refractive state was determined by failure to respond to routine management on moderate (125-150 gm.) carbohydrate diets.

These patients were all selected from the diabetic clinic of Charity Hospital of Louisiana at New Orleans. Like all patients in public institutions, all presented special problems. For the most part such patients come from the poorer classes of society, and serious economic and educational considerations enter into their treatment. These factors prevent the routine use of weighed diets, and frequently interfere with adequate insulin dosages. As a result, it is necessary in the majority of cases to use meas-

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ured diets, the accuracy of which is often doubtful.

Crystalline zinc insulin has been used in 20 refractive cases from the Charity Hospital Clinic, but only 14 patients have been followed sufficiently long to justify their inclusion in this report. Eleven have been followed from four to ten months on the new regimen, and three have been followed for two months.

The 14 patients had been managed at various times by various regimens as follows:

Eleven had been treated with protamine zinc insulin, four with two injections per day and the others with one daily injection.

Thirteen had been treated with regular insulin, two with four injections per day, nine with three daily injections, and two with two daily injections.

Nine had been treated with a combination of regular insulin and protamine zinc insulin, this form of therapy naturally requiring two injections per day.

No major changes were made in the diets during the period of observation. Two patients were hospitalized during the change to protamine zinc insulin, but the remainder were managed without difficulty in the clinic. The aim of our therapy was to keep the urine free from sugar, no consideration being given to blood sugar levels. That is, the patients were controlled almost entirely on the basis of their urinary excretion of sugar.

It was found that to achieve this result two doses of crystalline zinc insulin were usually necessary except in mild cases, with a total insulin requirement of 30 units or less, when one dose was sufficient. The larger of the doses was given from half an hour to an hour before breakfast, and the remainder half an hour before supper. The proportion of morning to evening dosage was maintained as nearly as possible at 2-3:1. The logic of this distribution is that more insulin action is required during the day, while carbohydrate absorption is going on, and only a sustaining dose is needed in the evening to insure aglycosuria during the night.

From the standpoint of the number of injections required crystalline zinc insulin did not fulfill the requirements of the ideal insulin preparation. It showed an advantage over regular insulin, but not over protamine zinc insulin.

Thirteen of the 14 patients treated with crystalline zinc insulin were controlled with two daily injections and the other required only one, whereas 11 of the 13 patients treated with regular insulin required three to four daily injections.

Seven of the 11 patients treated with protamine zinc insulin, on the other hand, required only one daily injection, and the others two daily injections, against the two daily injections required in 13 of the 14 patients treated with crystalline zinc insulin.

The nine patients who had been treated by a combination of protamine zinc insulin and regular insulin required two injections per day, just as they did on the crystalline zinc insulin regimen.

It is not possible to make a comparison of the total insulin dosage in the various regimens since the only time the patients were consistently aglycosuric was during their management with crystalline zinc insulin. It is interesting to observe, however, that:

Among the 13 patients who had been treated unsuccessfully with regular insulin, three required more crystalline zinc insulin, two the same amount, and eight less.

Among the 11 patients who had been treated unsuccessfully with protamine zinc insulin, six required more crystalline zinc insulin, one the same amount, and four less.

Among the nine patients who had been treated unsuccessfully with a combination of protamine zinc insulin and regular insulin, four required more crystalline zinc insulin, one was controlled with the same amount, and four required less.

From the outset the results of treatment with crystalline zinc insulin were most encouraging. Following the change to it, the glycosuria in all the patients, all of whom had proven refractive to control under other regimens, disappeared promptly and remained absent, except for a few isolated recurrences. In some instances it was possible to decrease the total insulin dosage as soon as the change to crystalline zinc insulin was made. In other instances a slight increase was necessary, which produced a disproportionate decrease in the 24-hour sugar excretion.

The charts are arranged, contrary to the usual custom, to demonstrate the additive disadvantages of various insulin regimens. Each column is a representative observation made during the

period in which one particular insulin regimen was employed, and the relationship between the various periods is shown by the relative heights of the columns under each heading.

The charts are constructed on the theory that the patient has the initial disadvantage of having diabetes with glycosuria and therefore requires dietary regulation. Other factors in his disease and its treatment introduce additional disadvantages. One is the necessity for taking insulin, with the resultant economic implications, and the fact that it must be taken by hypodermic injection. We have given equal weight to the amount of sugar excreted in the urine per 24 hours, and the total 24-hour insulin dosage. To the sum of these two factors, sugar excretion and insulin dosage, we have added an arbitrary third value, which represents each injection of insulin required, so that the total height of each column represents the total disadvantage to the patient of having diabetes at the time the particular observation was made.

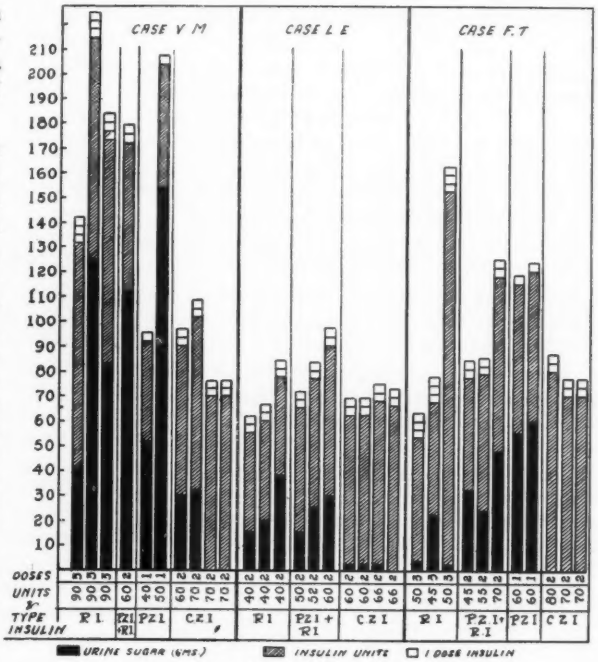

Chart 1

Control of glycosuria by crystalline zinc insulin in typical cases and relative disadvantages of various insulin regimens (V. M., L. E., F. T.).

It is evident that the most variable factor in this method of representation is the urinary excretion of sugar, which plays the dominant role in the changes depicted. This, we feel, is as it should be. Whatever one's attitude may be toward blood sugar levels, the chief aim of therapy in diabetes is to prevent glycosuria. The charts clearly demonstrate the ease and rapidity with which aglycosuria was induced by the change to crystalline zinc insulin in patients in whom other insulin regimens had been unsuccessful.

One patient, V. M., furnishes a particularly interesting demonstration of this fact. He is a colored man with active pulmonary tuberculosis,

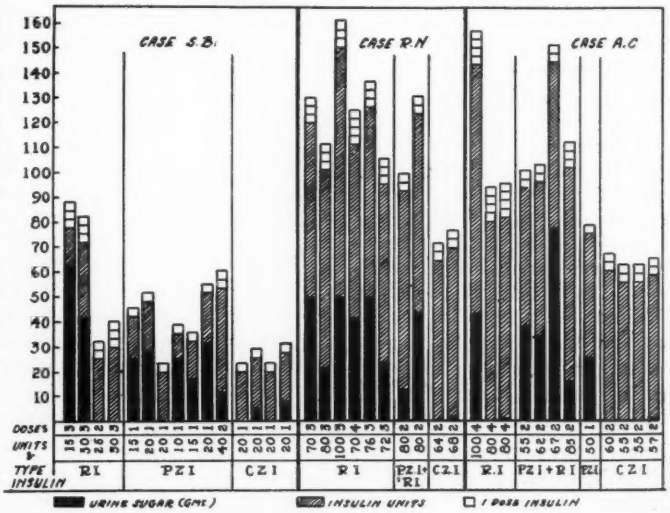

Chart 2

Control of glycosuria by crystalline zinc insulin in typical cases and relative disadvantages of various insulin regimens (S. B., R. N., A. C.).

who had proven extremely refractive to management on other regimens. On crystalline zinc insulin (*Chart 1*) his glycosuria rapidly decreased and finally disappeared entirely. In the three-month period since aglycosuria was first established, his urine has remained sugar-free, although during the entire period of observation there has been no evidence of any change in the activity of the tuberculous process.

Insulin reactions were observed in three cases. All occurred immediately following the change to crystalline zinc insulin, and apparently were caused by misjudging the individual insulin requirements.

The subsidiary question of insulin atrophy should be mentioned at this point, since several instances of this phenomenon have been reported as occurring with protamine zinc insulin, and we ourselves have observed two such instances. Similar reports have appeared concerning insulin atrophy following crystalline zinc insulin therapy.[14] Altshuler,[9] on the other hand, observed in three patients the disappearance of atrophy which had occurred under another insulin regimen when crystalline zinc insulin therapy was instituted. We have not observed the development of insulin atrophy during crystalline zinc therapy, but in two cases (*F. T., Chart 1; S. B., Chart 2*) we observed that when the change was made, atrophy induced by protamine zinc insulin progressed uninterruptedly.

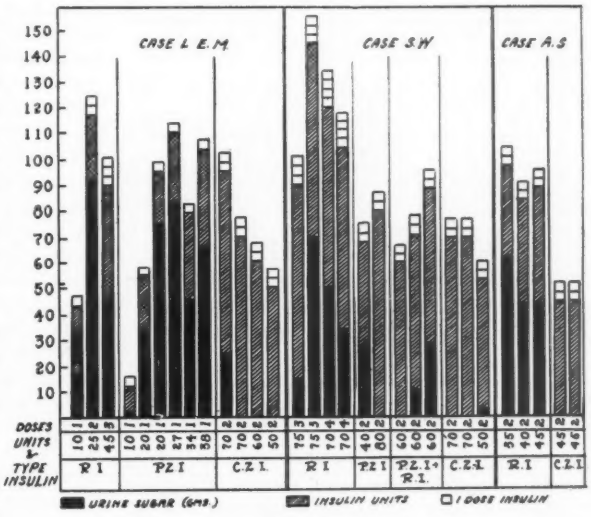

Chart 3

Control of glycosuria by crystalline zinc insulin in typical cases and relative disadvantages of various insulin regimens (L. E. M., S. W., A. S.).

SUMMARY AND CONCLUSIONS

(1) The action of crystalline zinc insulin was tested on 14 patients selected from a large diabetic clinic on the basis that their diabetic condition had not been satisfactorily stabilized on other insulins.

(2) These patients quickly responded to the change to crystalline zinc insulin, becoming aglycosuric at once and remaining so for periods of observation ranging from two to ten months.

(3) There was no great change in the total insulin dosage required. All but one of the 14 patients required two injections daily of crystalline zinc insulin, as compared with three to four injections of regular insulin and one to two injections of protamine zinc insulin, alone or in combination with regular insulin therapy.

(4) The development and maintenance of an aglycosuric state has been the outstanding advantage observed with the use of crystalline zinc insulin, and the total disadvantage to the patient of his disease and its treatment has thus been lessened.

(5) In spite of the brilliant contribution which modified insulins represent in the therapy of diabetes, the ideal insulin, adaptable to all cases, has not yet been developed.*

*We are indebted to Frederick Stearns & Co., Detroit, for the supply of crystalline zinc insulin used in this study.

REFERENCES

1. Lowe, R. C.; and Hampton, S. F.: Unpublished Data on the Treatment of More Severe Diabetes Mellitus with Protamine Zinc Insulin.
2. Boyd, J. D.; and Jackson, R. L.: Levels of Control in the Treatment of Diabetes Mellitus. J.A.M.A., **111**:906, 1938. Discussion by L. M. Boyer and P. A. Gray.
3. Allen, F. M.: Protamine Zinc Insulin and Treatment of Diabetes Mellitus. M. Times, **65**:608, 1937.
4. Soskin, S.; Allweiss, M. D.; and Cohn, D. J.: Influence of the Pancreas and the Liver Upon the Dextrose Tolerance Curve. Amer. Jour. Physiol., **109**:155, 1934.
5. Sahyun, quoted by Feinblatt, H. M.: Juvenile Diabetes Mellitus. Jour. Lab. & Clin. Med., **24**:337, 1939.
6. Hill, D.; and Howitt, F.: Insulin: Its Production, Purification and Physiological Action. Hutchinson Scientific Publications, London, 1936.
7. Freund, H. A.; and Adler, S.: The Effects of Standard, Protamine and Crystalline Insulin on Blood Sugar Level. J.A.M.A., **107**:573, 1936.
8. Mains, M. P.; and McMullen, C. J.: Clinical Investigation of an Improved Crystalline Insulin. J.A.M.A., **107**:959, 1936.
9. Altshuler, S. S.: The Clinical Use of Crystalline Insulin. Ann. Int. Med., **11**:901, 1938.

10. Altshuler, S. S.; and Leiser, R.: Clinical Experiences with an Improved Crystalline Insulin. J.A.M.A., **107**:1626, 1936.
11. Barach, J. H.: Crystalline Insulin. Ann. Int. Med., **10**: 1335, 1937.
12. Barach, J. H.: Experimental Studies on the Effects of Regular Insulin, Protamine Zinc Insulin and Crystalline Zinc Insulin. Penn. Med. Jour., **40**:349, 1937.
13. Shepardson, H. C.: and Friedlander, R. D.: Clinical Experiences with Long Acting Insulin in Ambulatory Diabetic Patients. Ann. Int. Med., **12**:830, 1938.
14. Beardwood, J. T.: Experimental Studies on the Effects of Regular Insulin, Protamine Zinc Insulin, and Crystalline Zinc Insulin (Round Table Conference). Penn. Med. Jour., **42**:379, 1939.

PROTAMINE ZINC INSULIN: SOME REASONS FOR OCCASIONAL DISSATISFACTION WITH ITS USE*

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Over five years have elapsed since Hagedorn and his co-workers first used protamine insulin in the treatment of diabetes mellitus. After thorough clinical trial by numerous physicians in various parts of this country for a period extending over a year, the improved modification, protamine zinc insulin, appeared commercially twenty-one months ago.

The fact has been stressed that, although final appraisal of the therapeutic results of protamine zinc insulin cannot be determined for perhaps many years, its immediate benefits make it the most valuable aid to the diabetic since the discovery of insulin. The opening of this new chapter in diabetic therapy, designated by Joslin as the Hagedorn era, has led to renewed interest in diabetes mellitus on the part of both the medical profession and the patients. Many reports have appeared in the literature, the majority of them indicating more favorable results with protamine zinc insulin therapy than with the use of unmodified or regular insulin alone. My own enthusiasm for the longer acting insulin is based upon experience with its use in 294 patients at the University Hospital and in private practice since June, 1936. The outstanding advantages are the greater convenience to the patient, the improved control of hyperglycemia and glycosuria and the increasing evidence that many of the more common complications have been and may be prevented.[1] Some unsatisfactory results have been reported, upon occasion in the literature, and more frequently by word of mouth from both patients and physicians. A careful analysis of events leading to the latter group of unfavorable experiences generally reveals that the impossible was expected or that certain important considerations associated with the use of protamine zinc insulin were not fully appreciated.

Injudicious dietary regulation or dietary indiscretions on the part of the patient account for many of the failures to maintain reasonable control of the glycosuria and hyperglycemia when protamine zinc insulin is used. Some dietary modification is necessary in successful regulation of every diabetic patient; it increases in importance when insulin is used. The latter part of the Banting era marked the advent of diets that were higher in carbohydrate, more adequate for the needs of the individual and simplified to a degree practical for patients of all economic levels. Although weighed diets are preferable, they are frequently impractical, and it has been our experience at the University Hospital, where all patients are instructed in measured diets, that excellent results may be obtained without the use of scales. Regularity of following a prescribed, adequate diet has been found to be far more important than the relative amount of carbohydrate and fat. The use of protamine zinc insulin has in no way eliminated the necessity for dietary regulation. On the contrary, certain adjustments in the diet may mean the difference between good and poor results. The action of the insulin, continuing to some extent over forty-eight hours, makes it advisable that no period elapse exceeding eight or ten hours during which the patient does not receive food. For this reason I invariably advise a bedtime lunch for each patient receiving protamine zinc insulin, regardless of the size of the dosage. As a rule it consists of bread and milk and occasionally cheese or meat because of the slower and more prolonged absorption of the carbohydrate. Postprandial glycosuria may at times be eliminated by decreasing the content of a meal and giving it as a lunch two hours or so later. This may also prevent the occurrence of an insulin reaction between meals.

Unquestionably some of the failures to obtain good results with the use of protamine zinc insulin are due to insufficient consideration of the importance of the severity of the diabetes in the individual patient. At the University Hospital, in the summer of 1936, detailed study was made of the effect of protamine insulin in nineteen patients.[2] Early in this study it be-

*Read in General Clinical Session, Southern Medical Association, Thirty-Second Annual Meeting, Oklahoma City, Oklahoma, November 15-18, 1938.

came apparent that the severity of the diabetes, as indicated by the patient's response to the regular insulin, was a valuable index as to the ease with which he might be regulated on protamine insulin. Those with marked fluctuations and a "paradoxical rise" in the blood sugar levels proved most difficult and could not be controlled without the use of some regular insulin in addition to the protamine (*Chart 1*). On the other hand, the group in which there was little fluctuation of the blood sugar level was easily regulated with protamine insulin alone (*Chart 2*). There appeared to be a number of patients between these two extremes, who could be controlled with protamine insulin, but continued to have moderate fluctuations in the blood sugar level and frequent glycosuria (*Chart 3*). My attention was directed to MacBryde's[3] study in which he found it of practical value from the standpoint of dietary management tc classify patients as relatively insulin sensitive or relatively insulin resistant according to their response to insulin. It is, of course, impractical to study every diabetic patient in such detail, but it is of practical value to appreciate the different degrees of severity and response to insulin. As a rule the young diabetics or those of long standing, especially if the onset was in early life,

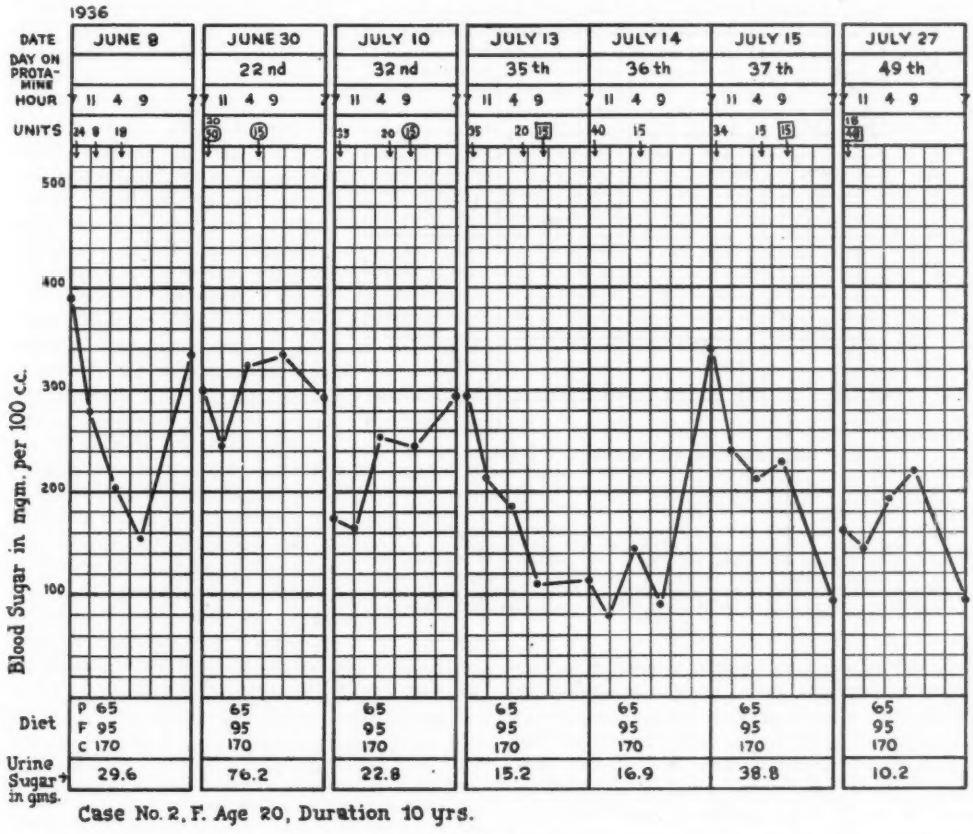

Chart 1

RELATIVELY INSULIN SENSITIVE (SEVERE)

Reasonable control could not be established with the use of unmodified protamine insulin alone. Fair control was obtained with regular insulin and a 9:00 p. m. dosage of 15 units of calcium protamine insulin. The increased efficiency of the calcium protamine insulin is noted in comparison of the graphs on July 10, 13, 14 and 15. Best control was established with a before-breakfast dosage of unmodified insulin and calcium protamine insulin. After it became available, protamine zinc insulin was substituted for the calcium preparation, and at the present time the patient is regulated on a dosage of 38 units of protamine zinc insulin, with 16 units of unmodified insulin before breakfast. The circled figures represent unmodified protamine insulin; those enclosed with squares represent calcium protamine insulin.

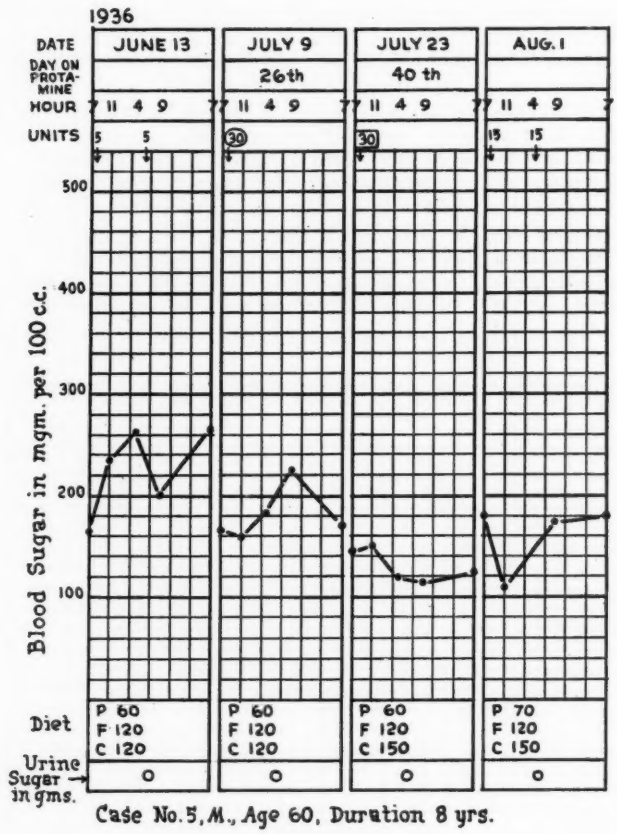

Chart 2

RELATIVELY INSULIN RESISTANT (MILD)

It will be noted that when receiving a dosage of 5-0-5 units of unmodified insulin the patient had no glycosuria, but the blood sugar level remained between 160 and 260. Thirty units of unmodified protamine insulin resulted in a definite reduction of the blood sugar level. When the same amount of calcium protamine insulin was administered the level was reduced almost to normal. Upon substition of the same number of units of unmodified insulin, the blood sugar level increased.

are more severe and frequently cannot be controlled without the use of regular or unmodified insulin in conjunction with protamine zinc insulin. Older diabetics, if more emotional than the average, may fall into this group. Fortunately, in 65 to 70 per cent of diabetics the onset is in the fifth decade or later,[4] and control with protamine zinc insulin may be obtained with comparative ease.

Not uncommonly a reported failure with protamine zinc insulin may be credited to incomplete consideration of details of administration and dosage, or an inadequate period of close observation of the patient during attempted regulation. It has been my experience, as well as that of others, that with only a rare exception, protamine zinc insulin and the regular insulin, if accessorily used, are preferably administered before breakfast. The dosage should not be changed too frequently and care should be taken to avoid rapid reduction of glycosuria with protamine zinc insulin alone. With the average uncomplicated patient, a reasonable degree of regulation may be obtained in ten to fourteen days. However, considerable change may occur in the ensuing few weeks, and, if possible, the patient should be seen at short intervals for at least six or eight weeks. When complications are not present, regulation through the office or outpatient department, rather than the hospital, is often preferable, since the patient's customary habits with reference to meals and activity are more normally maintained. The urine may be examined for sugar by the patient at definite periods four or five times daily; 24-hour quantitative estimations with the Sheftel set are helpful. As a rule, the fasting blood sugar gives the most valuable information as to the adequacy of the protamine zinc insulin dosage. Such estimations should be obtained as necessary and especially as the before-breakfast glycosuria disappears. Detailed instruction of the patient and individualization of treatment, with reference to activity and time of meals, are of vital importance.

R. H., a male sophomore college student 19 years of age, was first diagnosed as having diabetes mellitus September 15, 1938, about three weeks after developing the classical symptoms. His paternal aunt had died in diabetic coma 23 years before, at the age of 19. Physical examination was essentially unimportant except for the appearance of recent weight loss. His height was 5 feet 11 inches and he weighed only 126 pounds, about 25 pounds below his average. Regulation was established through daily visits to the office without his missing a single class and without cessation of his outside work as student janitor between the hours of 5:00

and 11:00 p. m. Since he played basket ball every afternoon for one to two hours and because of his work, an unusual schedule of meals was necessary. On October 8 the fasting blood sugar was 118 mg. per cent. By October 26, he had gained 25 pounds. He was receiving 18 units of protamine zinc insulin daily and for the preceding week had shown a trace of glycosuria in only 6 out of 28 urine tests. He had not experienced symptoms of hypoglycemia and was receiving the diet designated in *Table 1*. Five blood sugar estimations on that day are noted. Although clinical hypoglycemia had not been experienced during the 24-hour period, the blood sugar level was obviously lower than desirable. The insulin was reduced to 12 units. On November 9, the fasting blood sugar was 71 mg. per cent; he had received 12 units daily for the preceding week, during which time the urine remained sugar-free before meals and at bedtime. At the present time he is receiving 9 units of protamine zinc insulin before breakfast and only occasionally shows a mild glycosuria.

Regular insulin remains essential in the diabetic control of many patients receiving protamine zinc insulin. As previously noted, it is necessary in the majority of severe or relatively insulin sensitive patients. In the prevention of acidosis associated with infections its use is indispensable. I have seen a number of patients in diabetic coma who had previously been regulated with protamine zinc insulin. In each instance, whether due to dietary indiscretion or infection, coma might have been avoided had the patient or physician realized the urgent necessity for supplemental doses of regular insulin. The rapidity of the development of coma in children, especially in the presence of infection must not be forgotten in spite of some increase

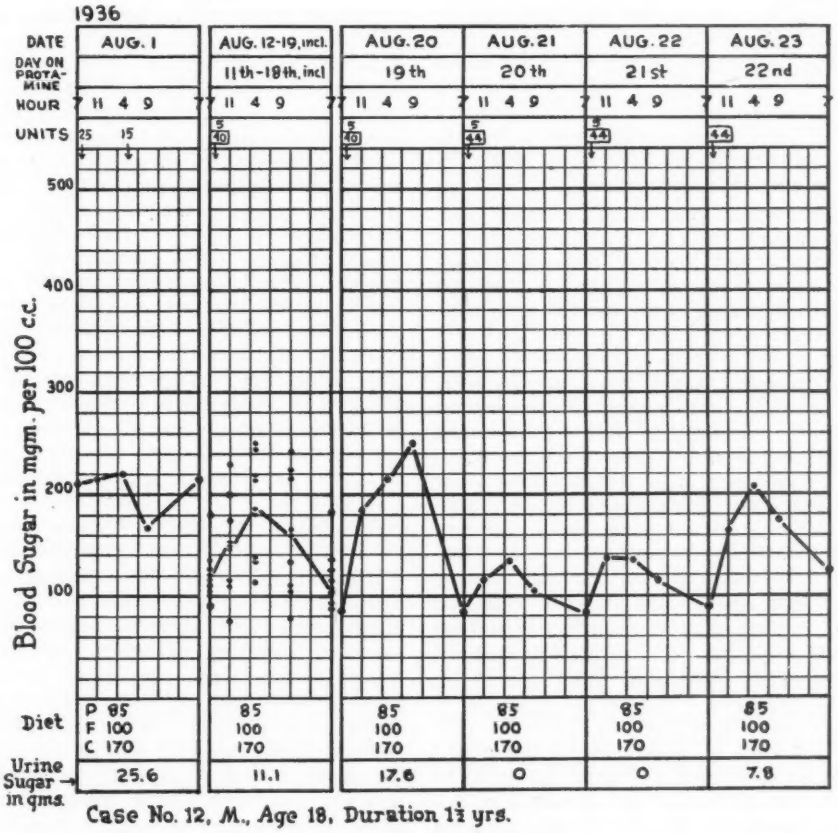

Chart 3

RELATIVELY INSULIN SENSITIVE (MODERATELY SEVERE)

The graph represents improved control after an increase of 4 units in the dosage of calcium protamine insulin. Upon omission of the 5 units of regular insulin, moderate glycosuria and hyperglycemia recurred.

R. H., A WHITE MAN, AGED 19, FORTY-ONE DAYS AFTER DIAGNOSIS AND BEGINNING OF TREATMENT WITH PROTAMINE ZINC INSULIN

10/26/38 Hour	Blood Sugar Mg. Per Ct.		Diet C.	P.	F.	Activity
7:15 a. m.	64	7:30 a. m.	52	22	30	
12:00 noon	74	12:15 p. m.	65	31	28	School
3:30 p. m.	70	4:00 p. m.	67	33	30	Plays basket ball
5:10 p. m.	89	7:30 p. m.	25	15	20	Janitor work
11:10 p. m.	60	11:30 p. m.	25	9	17	
Total diet (2426 cal.)			234	110	125	

24-nour urine specimen, no glycosuria.
18 units P.Z.I. before breakfast.

Table 1

in the margin of safety with the use of the longer acting insulin. One of my eight-year-old patients had his usual dose of 26 units of protamine zinc insulin and 8 units of regular on the morning he developed measles. At 4:00 p.m. the mother found no glycosuria; at 9:00 p. m. he had a brick red test and was vomiting; by the time he had reached the hospital at 1:00 a. m. he was in a severe diabetic coma.

The incidence of hypoglycemic reactions associated with the use of protamine zinc insulin, although slightly less frequent than with regular insulin, deserves special emphasis. There are important differences in the time of occurrence, cause, and symptoms which have been attributed to longer action of the protamine insulin. As a rule, hypoglycemia occurs late in the afternoon, during the night, or very early in the morning. Exercise acts more frequently as a precipitating factor and may result in a delayed reaction which occurs several hours or even a day later. The hypoglycemic symptoms are recognized with greater difficulty since they are often less abrupt in onset than those from regular insulin. Their characteristics differ in that headache, nausea, and an unpleasant disposition are common; vomiting may add confusion to the differentiation from acidosis. Other symptoms may be drowsiness, restlessness, paresthesias of the extremities, sweating, and hunger. In arteriosclerotic individuals, vascular episodes and even death have been attributed to hypoglycemia.[5] However, the possibility of increased severity of reactions from protamine zinc insulin need not prejudice against its use; for in most instances they may be avoided. During the period of early regulation, care must be exercised to refrain from too rapidly increasing the dosage or attempting to control postprandial glycosuria that may be eliminated by the administration of a small dosage of regular insulin or rearrangement of the diet. A special effort must be made to educate the new and re-educate the old patient as to the recognition of symptoms and the necessity for extra food to take care of extra physical activity. He should also understand the danger of delayed meals and the purpose of the bedtime lunch of slowly absorbed carbohydrates. The treatment of the early symptoms also requires emphasis since protamine zinc insulin reactions tend to recur. Fruit juice or some other form of quickly absorbed carbohydrate should be taken immediately and repeated in 20 or 30 minutes. If an hour or more intervenes before the next meal, this should be continued or followed by a lunch of bread and milk. Recently one of our patients ignored a late afternoon headache because it was almost time for her evening meal. Following the meal the headache was not relieved and she was unable to retain her dinner. Orange juice soon relieved the symptoms.

It has been experienced that diabetics who are well controlled with protamine zinc insulin develop greater improvement in their carbohydrate tolerance than they did when controlled with regular insulin alone. One of the earliest patients regulated with protamine insulin in the out patient department had failed to return for her usual visits until recently because she had been feeling well and showing no glycosuria. *Table 2* indicates the lower fasting blood sugar, compared to representative readings found on former visits. Joslin[1] has recently emphasized the danger of reactions and has cautioned us, "Al-

K. S., A WHITE WOMAN, AGED 64, ONSET OF DIABETES AT AGE OF 60. PROTAMINE ZINC INSULIN TREATMENT STARTED JANUARY 6, 1937

Date	Units P.Z.I.	Fasting Blood Sugar
February 10, 1937	44	160
August 18, 1937	44	181
November 10, 1937	44	86
May 4, 1938	41	155
November 9, 1938	41	61

Table 2

ways bear in mind a diabetic may improve and need a reduction in insulin, particularly an old diabetic or any diabetic who is doing unusually well."

SUMMARY

Unsatisfactory results with the use of protamine zinc insulin may often be attributed to one or more of the following:

(1) Injudicious dietary regulation or dietary indiscretions on the part of the patient.

(2) Insufficient consideration of the importance of the severity of the disease in the individual patient.

(3) Incomplete consideration of details of administration and dosage, or an inadequate period of observation during attempted regulation.

(4) Failure to use regular insulin in an accessory or supplemental way when indicated.

(5) Failure to recognize the difference in the time of occurrence, cause, symptoms, treatment, and prevention of hypoglycemia with protamine zinc insulin as compared to regular insulin.

CONCLUSION

The increased convenience to the diabetic patient and the improved control of his disturbed metabolism with protamine zinc insulin therapy should stimulate the physician and the patient to cooperate in its more widespread use and the avoidance of its dangers.

REFERENCES

1. Joslin, E. P., *et al.*: Protamine (Zinc) Insulin. Med. Clin. N. Amer., **711**:735 (May) 1938.
2. Keltz, Bert F.: Experience with the Use of Protamine Insulin. Jour. Okla. State Med. Assn., **30**:438-440 (Dec.) 1937.
3. MacBryde, Cyril M.: Response to Insulin as an Index to the Dietary Management of Diabetes. Jour. Clin. Invest., **15**: 577-589 (Sept.) 1936.
4. Joslin, E. P.: Treatment of Diabetes Mellitus, p. 35. Philadelphia: Lea & Febiger, 1937.
5. Danger of Protamine Insulin. Editorial, J.A.M.A., **111**: 254 (July 16) 1938.

PATHOLOGICAL NASAL CONDITIONS AFFECTING CLINICAL ALLERGY*

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Developments during the past two decades have forced the otolaryngologist to the realization that clinical allergy must be considered in 40 per cent of the patients that come to his office. The passing years have demonstrated the convergence of the two fields, and a comprehensive understanding of the fundamentals of one field is necessary for the clinical application in the other.

The most important factor in the treatment of any affection of the respiratory tract is the re-establishment of as nearly normal physiologic function as possible. The first logical step in this direction is restoration of normal anatomy. During the last few years much attention has been paid to the physiology of the nasal mucous membrane, and contributions of inestimable value have been made by Proetz,[1] Lierle[2] and others.

We now know that the maintenance of the integrity of the mucous blanket and the adequate functioning of the nasal cilia are the prime factors in combating infection in the nose. We also know that proper warming and humidifying of inspired air is essential, and that failure of these factors will be reflected in the entire respiratory tract.

Obviously, then, our attention is drawn to anatomical abnormalities. Septal deflections, spurs, enlarged turbinates, and polypi disturb the normal pattern of the air routes, causing drying and crusting on exposed points, excessive accumulation of secretions in other areas, with improper aereation and drainage of the sinuses, and inevitably leads to infection.

The observations on the incidence of deflected septa and polypi in asthma and seasonal hay fever made by Smith[3] and Alexander[4] are interesting and agree with our own experience. Smith observed deflected septa in 22 per cent and polypi in 9 per cent of 500 asthmatics.

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Alexander found 15 per cent deflected septa and 7 per cent polypi in 243 cases of seasonal hay fever. While we have actually advised submucous resection in possibly 2 per cent of cases, we believe that 10 per cent would more nearly approach the number who would receive material benefit by this procedure properly done. At least one of us does not accept the oft-repeated statement that skin reactivity is not a fair indicator of the degree of sensitivity of body cells to an allergen. It has been observed too often for coincidence that the person who, by skin test, is only mildly sensitive yet suffers acutely from hay fever in spite of estimated adequate treatment, frequently has small air ways, marked septal deviation, or polypi. In other words, a little swelling goes a long way with him in the direction of discomfort. It is only common sense that, if the edema cannot be entirely prevented, and usually it cannot, the patient will be more comfortable if he can be given more room for the swelling. Clinical experience with surgery directed toward this end bears out this conclusion.

We must not forget the occasional patient who gives a beautiful history of symptomatic hay fever, but who, after a more complete history and observation, is found not to be an allergic person at all. The allergist may be chagrined to learn that this well simulated hay fever can be explained on the basis of a septal spur which comes in contact with the mucous membrane of the lateral wall, causing the pseudo hay fever syndrome.

Submucous resection in an allergic nose is one of the most valuable surgical procedures the otolaryngologist is able to offer. An improperly done or partial submucous, on the other hand, not only fails to benefit the patient as it should, but renders a subsequent complete operation very difficult. The usual causes of failure in submucous resection are (1) inadequate removal of the perpendicular plate of the ethmoid and inferior ridges and spurs, (2) insufficient skill of the operator, (3) attempt to operate under general anesthetic, and (4) desire for speed. In patients with a narrow nose, and even a minor deviation of the septum, it is obvious that a minimal swelling will result in contact of the septal membrane with that of the lateral nasal wall. The turbinates on the side of the concavity hypertrophy in compensation, which in effect reduces the air way of this chamber to the same extent as that of the other side.

Following a complete submucous resection, it is often necessary and desirable to reduce the size of these enlarged turbinates by one of two methods, depending on the amount of swelling: (1) resection surgically of redundant inferior and medial portions of the inferior turbinate and removal of a part of a large anterior tip of the middle turbinate; (2) cauterization, which in some cases may produce a sufficient amount of fibrosis to shrink these bodies and provide adequate air way.

In the class of patients seen in private practice, it is unusual for the patient to procrastinate until extensive polypoid degeneration with marked infection has occurred in the ethmoidal labyrinth. For this reason, when polypi are encountered they are usually lying free in the middle or superior meatuses with their pedicles either in the ethmoid or maxillary sinuses. These redundant pouches of nasal mucous membrane are removed for one reason only: to provide free breathing space and facilitate aeration and drainage of the sinuses. The so-called reflex arc established between the ethmoidal region via the vagus to the bronchial musculature may exist, but we feel that this is not the essential pathogenesis of asthma. After such mechanical obstructions are removed, conservative measures are instituted, aimed at the eradication of infection in the ethmoids and sphenoids. Proetz displacements, using 0.5 per cent ephedrine in normal saline plus the judicious use of nose drops, will in most cases suffice.

In respect to nasal medication, we feel that, in the light of the newer knowledge of nasal physiology, any drug except 1 per cent ephedrine in saline or 0.25 per cent levo-meta-hydroxyphenyl - ethanol - methylamine hydrochloride ("neosynephrine") is absolutely contraindicated if it is to be used repeatedly. Many cases of lipoid pneumonia from oily nose drops have recently been reported, and the deleterious action of silver preparations, menthol and camphor has been conclusively demonstrated. In addition, the fact should be stressed to the patient that self-medication over a period of time will produce pathologic changes even in the normal nose.

We do not attempt to estimate the percentage of asthmatics who have sinus disease. Various figures are given in the attached table; and others reviewed, but not given here, add nothing but confusion to the whole.

Vaughan[13] estimates that 71.2 per cent of his cases have gross evidence of nasal disease and

INCIDENCE OF SINUS DISEASE IN ASTHMATICS

Author	Per Cent Infection	Remarks	No. Cases	Reported
Gottlieb[5]			117	1925
Adam, James[6]	68		850	1926
Rackeman and Tobey[7]	44-65		1007	1929
Chobot[8]	41	X-ray and clinical progress	100	1930
	63			1933
Smith. A. S.,[9] loc. cit	76	Diagnosis by x-ray	500	1932
	36	Direct inspection	500	1932
Kern and Schenck[10]	70	Clinical evidence	400	1933
	87.5	X-ray		
Cooke[11]	38	Ages 10 to 30	257	
	65	Ages 30 to 50	171	1935
	83	After 5	42	
Cooke and Grove[12]	92		248	1935

that half of his chronic asthmatics require adjustment of these conditions. Carmody and Greene[14] go so far as to say:

"We take the stand that without infection in the sinuses or without pathologic membranes, our irritants such as dusts, pollens, bacteria, foods, emanations of all sorts, etc., do not produce the so-called allergic coryza of hay fever."

Thus, estimates vary so widely as only to prove the utter worthlessness of statistics, the compilation of which is subject to individual prejudices and experiences.

We do not feel from our experience and from those of others that any one procedure can be depended upon to diagnose an infectious basis for any case of asthma. Infection may be as important in atopic asthma as in the cases believed to be purely infectious. Certainly history and observation of progress give us more accurate information in diagnosis than all other means.

The value of a complete history is demonstrated particularly in the cases of infected asthma. In childhood the onset is insidious because it is usually superimposed on an atopic diathesis. In the adult, on the other hand, two distinct types of history will be elicited, either of which strongly suggests the diagnosis. The one will have a long history of repeated asthmatic attacks or other allergic manifestations with a sudden disappearance of remissions. The other will have a completely negative allergic history until asthma develops, usually following an acute respiratory infection. We consider the former an infected asthma, the latter infectious asthma.

Progress of the case, however, is the final indicator that nasal pathology affects the asthma. Continued asthma with little variation from day to day in spite of allergic treatment is presumptive evidence of trouble above. Additional important information is revealed by repeated cytologic studies of the nasal secretions and sputum, as emphasized by Hansel. The presence of a large number of polymorphonuclear cells with or without eosinophils in the nasal smear indicates the presence of infection. Many interesting slides have been made on the sputum in infectious asmatics. Many bacteria are found both free and phagocytized by the white cells. Although this is not demonstrable in every case, we feel that when we find many intracellular bacteria, infection is playing a major etiological role. The actual percentage of eosinophils is not regarded as having much significance.

The first step in an allergic study is a detailed history, not taken on a form by an office assistant, but by the physician himself, for the personal contact between physician and patient establishes rapport and may bring to light many obscure facts which otherwise would not be elicited. Skin tests and study of the nasal secretions also form an essential part of the preliminary examination. It is our belief that the practicing allergist should, by all means, train himself to do a fairly complete rhinoscopic examination.

Unless immediate otolaryngologic problems

are present, the patient is started on his allergic regime before he is referred to the rhinologist. In this way, the latter has the complete allergic data at hand and may then recommend such measures as are indicated. Any surgery is deferred until the allergic study is completed.

There are no hard and fast rules applicable to the diagnosis of operable sinus disease in allergy. Sinusitis affects asthma in two ways, first by direct extension of infection, and secondly by causing nasal obstruction which results in mouth breathing. Nasal blockage allows unconditioned air to exert its irritating effect on the bronchial mucosa, and permits a greater concentration of allergens which ordinarily are filtered by the nose.

The criteria used for surgical intervention are essentially the same as for non-allergic patients, with the exception that lesser degrees of deviation of the septum are considered operative cases because of the swelling of the nasal mucous membrane, and maxillary antra are irrigated with fewer diagnostic clues.

X-ray studies of the maxillaries are of relatively little value, the thickened membrane causing an opacity which on the subsidence of the allergic attack will return to normal.

The sequelae of radical sinus surgery are at many times worse than the original condition, and this is particularly true in those individuals whose allergy is not perfectly controlled. Much of the condemnation of sinus surgery by the profession and the laity is justifiable, for the cases that are brought to their attention are those in whom overenthusiastic radical surgery has been done.

In a large series of cases in which the authors have collaborated, we have not felt the need for one single radical operation on an asthmatic. Intranasal antral windows, submucous resections, cauterization or resection of turbinates, removal of polypi, plus adequate allergic control and conservative local nasal medication have given very satisfactory results in those patients who have come to surgery. We do not infer that all of our asthmatics are relieved, and we recognize that permanent cures in asthma are always doubtful. We can expect good results in indirect ratio to the length and severity of the asthma. Our procedure does not essentially differ from those previously outlined by Dean[15] and Vaughan.[16] Intranasal antral windows, submucous resection, removal of polypi have not solved the problem of infectious or infected asthma. We are convinced, however, that the help afforded by these conservative procedures is greater than that given by radical surgery, and is not attended by the unhappy sequelae. Radical sinus surgery is to otolaryngology as panhysterectomy is to gynecology: a necessary evil and a last resort.

In conclusion, we wish to emphasize the following:

(1) The progress, with studies of nasal and bronchial secretions, gives us the only reliable means of diagnosing infected and infectious asthma.

(2) A submucous resection properly done is of great benefit in a large percentage of cases of hay fever and asthma.

(3) In sinus disease, conservative surgery is preferable, and offers good results in inverse ratio to the duration and severity of the asthma.

BIBLIOGRAPHY

1. Proetz, A. W.: Effects of Certain Drugs on Living Nasal Ciliated Epithelium. Ann. Otol., Rhinol. & Laryngol., **43**: 450, 1934. Five Preliminary Notes on Nasal Function. Ibid., **41**:1117, 1932: Studies of Nasal Cilia in the Living Mammal. Ibid., **42**:778, 1933. Nasal Ciliated Epithelium with Special Reference to Infection and Treatment. Jour. Laryng. & Otol., **49**:557, 1934.
2. Lierle, D. M.; and Moore, P. M.: Effects of Drugs on Ciliary Activity of Mucosa of Upper Respiratory Tract. Arch. Otol., **19**:55, 1934. Further Studies of the Effects of Drugs on Ciliary Activity. Ann. Otol., Rhinol. & Laryngol., **44**:671, 1935.
3. Smith, A. S.: Nasal Pathology Associated with Bronchial Asthma. Penn. Med. Jour., **35**:607, 1932.
4. Alexander, M. P.: Hay Fever and Its Complications. Penn. Med. Jour., **35**:605, 1932.
5. Gottlieb, M. J.: Relation of Intranasal Disease in Production of Bronchial Asthma. J.A.M.A., **85**:105 (July 11) 1925.
6. Adam, James: Asthma, p. 97. St. Louis: C. V. Mosby Co., 1926.
7. Rackeman, F. M.; and Tobey, H. G.: Studies in Asthma. IV. The Nose and Throat in Asthma. Arch. Otolaryngol., **9**:612 (June) 1929.
8. Chobot, R.: The Incidence of Sinusitis in Asthmatic Children. Amer. Jour. Dis. Child., **39**:257 (Feb.) 1930.
9. Smith, A. S.: loc. cit.
10. Kern, R. A.; and Schenck, H. P.: Chronic Paranasal Sinus Infection: Relation to Diseases of the Lower Respiratory Tract. Arch. Otolaryngol., **18**:425 (Oct.) 1933.
11. Cooke, R. A.: Infective Asthma: Indication of Its Allergic Nature. Amer. Jour. Sci., **183**:309, 1932.
12. Cooke, R. A.; and Grove, R. C.: Relation of Asthma to Sinusitis with Special Reference to Results from Surgical Treatment. Arch. Int. Med., **56**:779 (Oct.) 1935.
13. Vaughan, W. T.: Some Rhinological Aspects of Allergy. Jour. Allergy, **4**:127 (Jan.) 1933.
14. Carmody, T. E.; and Greene, L. W.: Relation of Sinus Disease to Hay Fever. Ann. Otol., Rhinol. & Laryng., **38**: 759 (Sept.) 1929.
15. Dean, L. W.: Relationship Between Diseases of the Nose and Throat and Pulmonary Disease. Mo. Med. Jour., **31**:13, 1934.
16. Vaughan, W. T.: Some Rhinological Aspects of Allergy. Jour. Allergy, **4**:127 (Jan.) 1933.

DISCUSSION (*Abstract*)

Dr. French K. Hansel, St. Louis, Mo.—Drs. Agar and Cazort are to be commended on the conservative manner in which they have managed their nasal problems. They have rightfully placed a great deal of emphasis upon the value of the cytologic studies in these cases. Cytologic

examinations of the nasal secretions are of value not only in diagnosis, but also in determining whether or not infection is a complicating factor. In uncomplicated cases, the nasal secretions show many eosinophils and when infection is present, a large number of neutrophils are found. In the acute infections the eosinophils may disappear and the cytologic picture may be entirely neutrophilic. In the management of respiratory allergy in children, we have found that the cytologic responses of the secretions are an accurate guide in determining the clinical course of the allergy, for when an exacerbation of symptoms occurs, it is always a question as to whether it is caused by allergic contact or by an acute infection. In these instances, the history is often indefinite, especially when there is no sore throat or fever. The examination of the nose may not show a marked hyperemia and the secretions may be mucoid rather than purulent. When an acute infection is superimposed on a nasal allergy, the secretion is so profuse and cellular dilution so high that a purulent appearance may never occur. It is evident, therefore, that accurate diagnosis can often be made only by microscopic examination.

Among otolaryngologists, there still exists a great deal of difference of opinion regarding the treatment of nasal polyps. In the management of these cases we have always used conservative methods. In the first place, the allergic state should be thoroughly investigated and the patient treated by allergic methods before considering the removal of polyps. With the control of symptoms there may be a marked reduction in the size of the polyps or they may completely disappear. If the allergic symptoms are controlled and there is no change in the nasal polyps, certainly they should be removed. On the other hand, if they are removed when the nasal symptoms have not been controlled, there is likely to be a recurrence. Acute edematous polyps are not infrequently seen in hay fever cases. They usually disappear after the hay fever season. Temporary edematous polyps may also occur during an acute infection, but they usually disappear when the infection subsides. The resorption of edema in nasal polyps is dependent upon the control of the allergic reactions. In those instances, however, in which marked fibrosis has occurred in the polyps, there is likely to be little change even after the allergic symptoms have subsided.

In nasal polyp cases a moderate number of neutrophils in addition to eosinophils are usually found in the secretions. The presence of neutrophils is the result of the stagnation of secretions in the nose and sinuses. After control of the allergic symptoms and possibly the removal of polyps, ventilation of the sinuses is usually restored and the stagnation of the secretion disappears. Although the secretions may then show many eosinophils, there are few, if any, neutrophils. In many cases of nasal polyps, therefore, the secondary infection is the result of a stagnation process rather than a true complicating suppuration. Definite infection usually occurs in those cases in which the pathologic changes in the sinuses are characterized by cystic degeneration. Localized abscesses in the mucosa may occur.

Dr. Agar (closing).—There are two things I want to mention relative to the diagnosis of sinusitis in children. Men who are confining their practice to allergy and not doing nose and throat work are not going to be able to recognize the symptoms of sinusitis in children so easily as in adults, as they are not going to have the localized headaches and other symptoms which are ordinarily present in adults. Sinusitis in children is suspected when there is an increase in asthmatic symptoms, when they have colds which continue over a long period of time, repeated attacks of otitis media, and by the presence of cough. If any, or all, of these are present, sinusitis should be strongly suspected.

Dr. Hansel, Dr. Cazort and I mentioned that the allergic study should be made before any surgery is contemplated, but we must remember that the patient's first interest is in breathing. For this reason surgery should not be deferred too long, for frequently a complete allergic study requires a considerable period of time during which the patient becomes discouraged and is apt to condemn both the allergist and rhinologist for not alleviating his chief complaint.

THE ORIGIN AND TREATMENT OF SUBPHRENIC INFECTIONS*

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Of all the complications arising in the practice of medicine, a localized collection of pus in contact with the under surface of the diaphragm is one of the most difficult with which we have to deal. Being essentially a localized peritonitis, it is practically always preceded by disease elsewhere in the body. There are few signs and symptoms which are definitely pathognomonic of subphrenic abscess; and of the varied symptoms which may be present, part may be actually misleading. It is on account of this fact, and the obscurity of the signs, that many cases remain undiagnosed until operation or autopsy. If the condition goes unrecognized until diaphragmatic perforation takes place, both the difficulty of diagnosis and gravity of prognosis are increased, since one is then confronted not only with a subphrenic infection, but also with a pyopneumothorax, the physical signs of both being identical in many respects. Subphrenic abscess by itself carries a mortality of from 20 to 40 per cent, and since the treatment of this condition is wholly surgical, the necessity for early diagnosis is apparent.

Barnard,[1] in his paper of 1908, has given a good classification of subphrenic abscess based upon the anatomy of the subphrenic region. Subphrenic infection is usually intraperitoneal in location. Although it is rare in occurrence, the infection may begin in the extraperitoneal

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spaces beneath the diaphragm, namely, between the layers of the ligaments over the dome of the liver. The intraperitoneal subphrenic area is divided into right and left portions by the falciform ligament, and these in turn are divided into anterior and posterior spaces by the lateral ligaments.

Since the extraperitoneal space is divided into right and left portions, we have four intraperitoneal, and two extraperitoneal spaces where a subphrenic abscess may localize. The right anterior subphrenic space communicates at its lateral and posterior liver margin with both the right posterior space or subhepatic pouch and the right lumbar space, lying between the ascending colon and the lateral abdominal wall. It is on account of this fact that infection may ascend into these spaces from the appendix, kidney, liver, stomach and duodenal regions. On the left, the anterior subphrenic space may receive infection, ascending from the pelvis by way of either the external lumbar, or the internal lumbar fossae. The left posterior space or the lesser peritoneal sac opens into the right posterior space by the foramen of Winslow, but this rarely serves as a route for infection spreading from one to the other, because it is usually sealed off by adhesions early in the process.

From these anatomical considerations, one would expect to find three main types of subphrenic abscess, namely: right anterior combined with right posterior, left anterior, and left posterior.

Subphrenic abscess almost invariably originates from lesions situated in the peritoneal cavity. Beye[2] found in a series of 190 cases of acute and chronic thoracic empyemata only one subphrenic abscess, and in this single case, transmission of the infection took place through a traumatized diaphragm. The fact that thoracic empyema practically never passes downward to the subphrenic space may perhaps be explained by the location of the nodes of the phrenic lymphatic system on the thoracic side of the diaphragm. Barnard, Piquand,[3] Ramsbottom,[4] and earlier writers, felt that peptic ulcer was probably the most frequent source of infection involving the subphrenic space; however, more recent date writers, namely, Ochsner,[5] Debakey,[6] Graves[7] and others, in an analysis of several hundred cases, have found the appendical source of infection by far the most common. Ochsner and Graves, in an analysis of 3,372 cases, found males to predominate in the approximate ratio of 3:1; 70 per cent of the cases were in the age period of the second to the fourth decade; the most important antecedent intraperitoneal lesion was the appendix. In a still more recent article, Ochsner and Debakey reported the most common organisms as colon bacillus, streptococcus, and staphylococcus; and the right posterior subphrenic space as the most frequent localizing area. In their analysis of 3,608 cases, this space was involved in 33 per cent.

The pathology of subphrenic abscess is the same as that of any other abscess in the body. However, a point which should be mentioned in this connection is the relationship between the position of the patient and the development of localized subphrenic infection. When a patient is lying in the dorsal position, the two kidneys and the perinephric fat form the highest points in the two paravertebral gutters; and hence in the early stages of peritoneal inflammation, that is the diffuse exudative stage, the subphrenic spaces may become involved simply through a gravitational flow from this region.

Except where the appendix occupies an unusual location, infection from this source is most likely to travel intraperitoneally along the paracolic groove on the right. The other most important method by which appendical infection may reach the subphrenic space is by a pyelophlebitis. In the cases where appendicitis is the primary lesion preceding subphrenic infection, the liver is usually found firmly bound to the diaphragm in front by numerous adhesions; and as the abscess develops in size, the diaphragm moves upward, compressing the base of the lung. Gas in the abscess will depend upon the infecting organism. Perforating ulcers of the anterior surface of the stomach and duodenum cause a generalized peritonitis from which localized portions may be later established in the subphrenic spaces. In these perforated lesions, a resulting pneumoperitoneum may cause an immediate backward and downward depression of the liver before adhesions to the diaphragm have had time to form; and if this happens, it may form a valuable sign in diagnosis. In perforated ulcer of the posterior wall of the stomach, the left posterior subphrenic space or lesser peritoneal sac is directly involved. If after a subphrenic abscess is formed and is left untreated, the most common and serious complication is perforation of the diaphragm, and the formation of a pyopneumothorax. Lockwood has reported that almost 42 per cent of the deaths in subphrenic abscess are due to intrathoracic complications of

this type. Another of the most serious complications is rupture into the peritoneal cavity. Rupture to the outside, into the colon, stomach, and other hollow viscera very frequently occurs.

The signs and symptoms of subphrenic abscess may present themselves from a few days to months after the causative lesion. Where appendicitis is the originating lesion, the time before the symptoms occur is usually drawn out, while following perforated peptic ulcers, the signs appear much sooner. Also as a general rule, the greater the operative delay in the antecedent appendical lesions, the quicker will the signs of subsequent subphrenic abscess become apparent.

Where the onset of subphrenic localization is sudden, the subsidence of the symptoms of the primary lesion and a normal temperature may be followed by severe pain in the chest, secondary septic temperature elevation, leukocytosis, enlarged liver dullness, friction sounds over the hepatic area and tenderness over the adjacent intercostal area. Ochsner and Graves feel that this intercostal tenderness over the twelfth rib or along the costal margin is most common. The x-ray findings of subphrenic abscess may include an elevated diaphragm on the affected side, subdiaphragmatic fluid with or without gas, diaphragmatic pleurisy with or without effusion, and compression of the lung base. Fluoroscopy shows decreased movements or even paralysis of the diaphragm. If the abscess contains gas, a shifting fluid level may be obtained, and if so, one has a sign practically pathognomonic of the condition. Exploratory aspiration has been used to confirm the presence of subphrenic pus, but it is not favored by many, namely, Lehman,[8] because of the danger of contaminating uninvolved serous cavities. Sante has suggested the use of induced pneumoperitoneum to prove whether a subphrenic area is clear or involved, but this procedure would not seem to be entirely safe because of the possibility of causing an intraperitoneal rupture of the abscess if present. Hussey[9] has reported such an accident. In consideration of the dangers of induced pneumoperitoneum and exploratory aspiration, the diagnosis of subphrenic abscess should rest upon the previous history, mode of onset, physical signs and symptoms and repeated x-ray and fluoroscopic examinations. When hiccoughing is present, Fagge feels that this is a valuable sign. After diaphragmatic perforation has taken place, there may be great difficulty in differentiating it from a thoracic empyema, but sudden cough, rapid respiration, expectoration, collapse and a depressed liver may help in settling the question.

The prognosis in subphrenic abscess depends upon the etiology, location, promptness with which the condition is recognized, and the type of treatment instituted. The mortality of cases not operated upon approximates 100 per cent, while that of the cases operated upon varies from 20 to 40 per cent, depending upon the type of treatment used. Lockwood says that 41.9 per cent of deaths due to subphrenic abscess are accounted for by intrathoracic complications. Ochsner and Graves report a 21 per cent mortality out of 189 patients who were operated upon by extraserous drainage methods, a 39 per cent mortality among 305 patients in whom transpleural drainage was used, and a 35.5 per cent mortality out of 307 patients where transperitoneal drainage was used. From these considerations, therefore, we may say that the lowest mortality figure will be obtained if the condition is recognized before thoracic complications take place, and if the extraserous drainage method described by Ochsner and Nathan is used.

Ochsner and Graves feel that only 30 per cent of subphrenic infections will progress to the formation of a subphrenic abscess, which will demand prompt recognition and surgical treatment. If one is not able to confirm the presence of a subphrenic abscess by the signs and symptoms present, but feels that they must be present, the question of exploratory operations arises.

E. P. Lehman[8] says that exploration is justified only as a court of final appeal, and that it must not be delayed too long. He further feels that of the three categories (subphrenic abscess, liver abscess and supraphrenic abscess), only the latter is likely to be harmed by exploratory operation, provided that the extraserous approach is used. Of the three methods of approach to a subphrenic abscess, transpleural, transperitoneal and extraserous routes have been used in the past. Mortality figures by either the transpleural and transperitoneal route have been upwards of from 35°to 40 per cent, while the extraserous method of approach has produced the lower mortality figure of 21 per cent. In using the transpleural route, the operation has been done in

two stages, the first stage consisting of approximating the diaphragmatic pleura to the parietal pleura of the thoracic wall. This method, however, does not always prevent contamination of the pleural cavity, either because of the insufficient density of the adhesions thus produced and because the patient may by coughing tear the pleural surfaces apart during the second stage of the operation. The transperitoneal route has been used where the abscess points in the epigastrium, which site incidentally may be that of the previous operation preceding the subphrenic involvement. Nathan and Ochsner[10] do not favor either the transpleural or transperitoneal route for drainage or even for aspiration, because of the great danger of contamination of an uninvolved serous cavity. They have described a method of retroperitoneal drainage, which is briefly carried out by incision laterally at the under surface of the diaphragm and separating the peritoneum upward along the under surface of the peritoneum until the abscess is reached. The authors point out that this type of operation not only avoids the possibility of creating a pyopneumothorax, but that it serves to drain the abscess at its most dependent point.

Amebic abscesses in the liver and subphrenic areas, Ochsner feels are best handled by repeated aspirations and the administration of amebicides rather than operative drainage which may introduce secondary infection with a subsequent toxemia.

CONCLUSIONS

(1) Subphrenic abscess, although relatively rare compared with other acute surgical complications, is important in that it offers special difficulties in diagnosis and treatment.

(2) The etiological cause is almost invariably pre-existing abdominal lesions, the most common being appendicitis, and next most common peptic ulcers. The method of subphrenic infection is ordinarily by direct extension.

(3) A large number of cases are recognized only at operation or necropsy due in part to inconstant physical signs and in part to too few x-ray and fluoroscopic observations.

(4) A pyopneumothorax is the most common serious complication of subphrenic abscess, and since nearly half the deaths of subphrenic abscess are due to intrathoracic complications, it is important that the condition receive prompt recognition and treatment.

(5) The lowest reported mortality has been obtained where the extraserous method of drainage has been used.

REFERENCES

1. Barnard: Brit. Med. Jour., p. 371, 1908.
2. Beye: Arch. Surg., **14**:240, Part 2, 1927.
3. Piquand: Revue de Chir., **39**:—, 1908; **40**:—, 1909.
4. Ramsbottom: Brit. Med. Jour., p. 5 (July 23) 1930.
5. Ochsner: New Orleans Med. & Surg. Jour., **582**:752 (May) 1930.
6. Ochsner and Debakey: Internat. Abst. Surg., **66**:428, 1938.
7. Ochsner and Graves: Ann. Surg., **98**:961 (Dec.) 1933.
8. Lehman, E. P.: Ann. Surg., **106**:514 (Part 2) 1937.
9. Hussey: Johns Hop. Hosp. Bull., **18**:86, 1919.
10. Nathan and Ochsner: Surg., Gyn. & Obst., p. 665, 1923.

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EDITORIAL DEPARTMENT

SOUTHERN MEDICAL ASSOCIATION
Thirty-Third Annual Meeting
Memphis, Tennessee, November 21-24, 1939

THE MEMPHIS MEETING

NOVEMBER 21-24

Those who were privileged to attend either one or both of the previous meetings of the Southern Medical Association in Memphis (1917 and 1927) will remember the manifest charms of that city.

DATE OF THE MEETING

For some thirty years it has been the policy of the Association to meet between election week and Thanksgiving week. In determining the date for the Memphis meeting, the officers of the local society expressed a preference for the third week of November, November 21-24. And since that date did not interfere with either election or the traditional Thanksgiving, it was selected as the meeting date.

The announcement of President Roosevelt suggesting that Thanksgiving this year be a week earlier caused considerable concern. Numerous obstacles stood in the way of any change of date for the convention. A large obstacle was the fact that engagements for the use of the necessary meeting place, the Municipal Auditorium, were completed nearly a year ago by the Southern Medical Association, and for other groups at other times. The officers of the Association, therefore, unanimously decided to hold to the original date. The Governor of Tennessee has announced that Tennessee will observe the traditional date, November 30, so the meeting will not be on Thanksgiving Day in Tennessee, even if it should be on Thanksgiving in some other states. Governors of Alabama, Arkansas and other Southern states have also indicated that they will observe the traditional date of November 30.

PROGRAM

The program for Memphis will follow in general the plan of recent meetings. Tuesday will be "Memphis Day," a program of short clinical presentations by physicians of Memphis. A General Clinical Session, a program arranged by the President, will be conducted on Wednesday morning. Beginning Wednesday, the nineteen sections of the Association and the three conjoint meetings will convene. A General Session featuring the address of the President, Dr. Walter E. Vest, of Huntington, West Virginia, followed by the President's Reception and Ball, will be on Wednesday evening. As usual, the alumni reunions will take place on Thursday night. On Tuesday evening there will be a public session, a program arranged for the laity.

The programs of the section and general meetings in Memphis are complete and promise generous and stimulating discussions of many phases of medical progress.

EXHIBITS

The scientific and technical exhibits have increased each year in number and in excellence. Scientific exhibits are presented only by physicians within the territory from which the Association draws its membership, or by the invited guest speakers of the sections. They display particularly the work of Southern physicians.

The technical or commercial exhibits will be of a high order. The Association is pioneering in a new policy regarding technical exhibits, a policy of no selling, no sampling and no souvenirs.* It is hoped that this policy will permit the physician to inform himself without being importuned to purchase; and will favor the advertiser by providing him with a larger audience

*Editorial: Technical Exhibits at Memphis Meeting. Sou. Med. Jour., 32:671, June, 1939.

to study his products. Physicians may, of course, at any time order any article which they may wish.

MUNICIPAL AUDITORIUM

Most of the scientific sessions, the technical and scientific exhibits, and the registration will be found in the Municipal Auditorium within comfortable walking distance of hotels. It will be necessary to go outside the Auditorium for some three or four meetings, which will be held in the religious education buildings of two churches, just one block from the Auditorium.

HOTELS

There has been an unusually heavy pre-meeting reservation at the hotels. Several hotels are already booked to capacity, but there are still good accommodations available. Those who have not already made hotel reservations should write to the Hotel Committee, Southern Medical Association, Box 224, Memphis.

TRANSPORTATION

Memphis is easily accessible from all points. It is a prominent railroad gateway with good train service in all directions. Several special trains are being arranged. Air lines north and south, east and west, stop in Memphis. Since Memphis is central and well supplied with good roads in all directions, many physicians doubtless will travel by automobile.

LOCAL MEDICAL SOCIETY

Memphis' very active local society, the Memphis and Shelby County Medical Society, has a membership of more than three hundred physicians. Its officers are: Dr. J. H. Francis, President; Dr. W. C. Chaney, President-Elect; Dr. W. D. Stinson, Vice-President; Dr. E. G. Kelly, Treasurer; Dr. A. F. Cooper, Secretary. Dr. W. L. Williamson is General Chairman for the Southern Medical Association meeting by appointment of the President, Dr. Francis.

OVARIAN FUNCTION AND EFFECT OF EXTRACTS

It becomes increasingly difficult to assign credit for new therapeutic methods. Modern treatment of pernicious anemia had its foundations in the studies of Whipple and Robscheit-Robbins on hemoglobin generation in bled dogs; and the therapy of pellagra with nicotinic acid was developed following protracted investigations on canine black tongue and the demonstration by Elvehem[1] and his associates that this disease is relieved quickly by nicotinic acid.

Modern knowledge of the hormones of the ovaries had its basis in the work of Stockard and Papanicolaou[2] at Cornell University in 1917 on cyclic changes in the vaginal structure of small animals. Allen and Doisy[3] in St. Louis in 1922 used Stockard and Papanicolaou's vaginal smear test to determine the activity or inactivity of commercial ovarian extracts (at that time practically all were inactive) and to concentrate and finally crystallize the follicle hormone theelin (Doisy, Veler and Thayer).

Cyclic changes in the human vagina as shown by the type of cells on its surface during ovulation, corpus luteum formation and in pregnancy were later described by Papanicolaou and Shorr,[4] and they suggest that vaginal smears may be used as a means of diagnosis of human menstrual disturbances, and for the evaluation of hormone therapy in women. The vaginal lining cells change, they say, to a characteristic follicular stage when adequate amounts of active estrogenic or ovary stimulating material are administered. They show histologic appearances of the follicular phase of the vaginal smear, in which large flat cells with small pyknotic nuclei predominate, and the menopausal picture with chiefly elongated cells. They describe the human vaginal reaction after treatment with several hormones, and the vaginal cells in primary and secondary amenorrheas.

The androgens (male hormones) suppress the menses and produce a picture of atrophy in the human vagina like that of the menopause. In certain amenorrheic young women, administration of the anterior pituitary-like extract of human pregnancy urine or pregnant mare's serum was followed by vaginal changes characteristic of the ovulatory phase; but the smears reverted regularly to the atrophic type after therapy was

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1. Elvehem, C. A.; Madden, R. J.; Strong, S. M.; and Wooley, D. W.: Relation of Nicotinic Acid in Nicotinic Acid Amide to Canine Black Tongue. Jour. Amer. Chem. Soc., **59**:1767 (Sept.) 1937.

2. Stockard, C. R.; and Papanicolaou, G. N.: Existence of a Typical Oestrous Cycle in the Guinea Pig, with a Study of Its Histological and Physiological Changes. Amer. Jour. Anat., **22**: 225, 1917.

3. Allen, Edgar; and Doisy, E. A.: An Ovarian Hormone. J.A.M.A., **81**:809, 1923.

4. Papanicolaou, G. N.; and Shorr, E.: Amer. Jour. Obst. & Gyn., **31**:806, 1936.

Shorr, Ephraim; and Papanicolaou, G. N.; Action of Gonadotropic Hormones in Amenorrhea as Evaluated by Vaginal Smears. Proc. Soc. Exper. Biol. & Med., **41**:629 (June) 1939.

stopped and spontaneous activity did not ensue. In these patients, a diagnosis of primary amenorrhea was made.

In the study of ovarian disorders, accurate differential diagnosis just now is more needed than therapy. A number of chemically pure pharmaceuticals or hormones are on the market which alter the genital structures considerably, but their clinical uses are poorly defined.

Diagnostic evidence of the type that may be obtained from the exfoliated vaginal cells is not difficult to obtain. It is much simpler to make and examine a smear than to do an endometrial biopsy or attempt to assay the quantity of hormone in a patient's blood or urine. It should be possible to obtain needed information about the ovarian function of women with either amenorrhea or metrorrhagia by repeated study of vaginal smears.

GLEANINGS FROM RECENT JOURNALS

Toxicity of Sulfapyridine.—After a year of exceedingly conservative study in medical centers, sulfapyridine was released for general use by the Federal Trade Commission. It is believed to be of value in certain pneumonias and in other diseases. Among the conditions in which it is not helpful is poliomyelitis.

Its toxic properties, though recognized, are said to be less than those of sulfanilamide and are not sufficient to offset its therapeutic usefulness; but undesirable reactions have been noted frequently enough to emphasize the need of caution and meticulous observation of the patient who is taking it.

Rosenthal and Vogel,[1] of New York City, report three cases of granulocytopenia in children in the past few months, with two deaths, following sulfapyridine. The ages of the children were one year, ten years and four years. The drug was given to all three over somewhat prolonged periods, or intermittently. The youngest patient received 8 grams in seven days and later 1.25 grams. He recovered. A patient of ten years received 95 grams in about two weeks and a patient of four years received 20 grams in a week, then 21 grams in a week, a total of 41 grams. Both of the latter died.

It is said that a hemolytic reaction, with drop in hemoglobin and the appearance of jaundice, is sometimes noted very early after administration of sulfapyridine. Granulopenia, in the experience of the New York writers, was a later development, after repeated use. They urge that the patient's blood be examined daily during treatment with sulfapyridine, so that the drug may be withdrawn at the earliest sign of diminishing leukocytes.

Molitor and Robinson,[2] of the Merck Institute, report the formation of uroliths in rats, rabbits and monkeys after oral administration of sodium sulfapyridine. The minimal dosage necessary to produce urinary concretions in these three species was 0.25 grams per kilogram in monkeys to 2 grams per kilogram in rats, administered daily for ten days.

Individual idiosyncrasy is such that it is hardly safe to permit this medicament to be taken by persons who are not being repeatedly examined by a physician, and it is necessary that the physician be alert to note any change which may indicate an unfavorable reaction.

Effect of One Vitamin Deficiency Upon Another.—The accessory food factors not only are necessary to life, but a given quantity is necessary in some instances for assimilation of a given number of calories. The thiamin requirement particularly is known to be increased by increasing other components of the dietary, such as protein.

Susceptibility to vitamin deficiencies varies considerably with the species of animal. In studies on scurvy, the standard animal is the very susceptible guinea pig. The rat is not subject to this disease, but is able to synthesize ascorbic acid on a vitamin-C-free ration. How it makes C is not known but, according to Barnett Sure[3] and his associates at the University of Arkansas, considerable reduction of the C content of rat tissues occurs during several other types of vitamin deficiency. The albino rat may either fast for ten days, or he may for the same period eat a large quantity of pure ascorbic acid, without notably altering the ascorbic acid content of his tissues.

However, during deficiency of vitamins A, B_1 and B_2, the C content of rat tissues is lowered. Repeated depletions of any of these factors in-

1. Rosenthal, Nathan; and Vogel, Peter: Granulocytopenia Caused by Sulfapyridine in Children. J.A.M.A., **113**:584 (Aug. 12) 1939.

2. Molitor, Hans; and Robinson, Harry: Toxic Manifestations After Oral Administration of Sodium Sulfapyridine. Proc. Soc. Exper. Biol. & Med., **41**:409 (June) 1939.

3. Sure, Barnett: Theiss, R. M.; and Harrelson, R. T.: Vitamin Interrelationships. Influence of Avitaminosis on the Ascorbic Acid Content of Various Tissues and Endocrines. Jour. Biol. Chem., **129**:245 (July) 1939.

creasingly depletes the tissues of C. Vitamin B_6 deficiency does not affect the rat content of vitamin C.

Following riboflavin deficiency (B_2) the greatest reduction of vitamin C occurred. The quantity in the liver, kidneys and lungs was reduced to about half normal. In the thymus it was reduced more than four-fifths. There was reduction in the ascorbic acid of the thyroid, but no change in the adrenals or pituitary.

The Arkansas authors ask whether in human beriberi or riboflavin deficiency the requirement of vitamin C may be increased. In human pellagra, a diet rich in vitamins is usually advised, in addition to specific treatment with nicotinic acid.

It is significant that one vitamin aids in maintaining in the vital organs another vitamin of quite different formula, and that the recently separated B components have entirely different physiologic effects in regard to vitamin C.

TWENTY-FIVE YEARS AGO

From Journals of 1914

Belgian Refugees in England.[1]—The allotting of refugees to the families that offer hospitality is a very delicate and difficult matter. The War Refugees Committee had already arranged for the reception of 3,500 refugees when the figure of arrivals began to attain to more than 300 per day * * * and the government consented to take the matter in hand. * * * Hospitality will have to be found for at least 100,000 at once. * * * An increasing proportion of the refugees are highly educated refined gentlemen and ladies * * * professors at universities * * * doctors of law or of medicine * * * large employers of labor * * * absolutely penniless * * * since the fall of Antwerp.

Members of the medical profession * * * have so wide a circle of acquaintances that it would be comparatively easy for them to discover families willing to offer hospitality to the better class of refugees.

Medical Journals in the Early Days of the War.[2]—To those who are accustomed to receive regularly the medical journals of continental nations now at war, their abrupt cessation with the outbreak of hostilities brings with it a curious sense of isolation. Whether the German weeklies are being printed we actually do not know, but correspondents in Switzerland indicate that some at least are still appearing. A letter from Paris published in the *Journal of the American Medical Association* * * * states that the *Semaine Medicale* has ceased publication and that the *Presse Medicale* is appearing as a sheet of medico-military information.

Recall of Carrel.[3]—Dr. Alexis Carrel, of the Rockefeller Institute for Physical Research at New York, is a citizen of France. He has returned to his country and has been sent to the front to serve as an army surgeon.

1. Special Sanitary Commission. Lancet, p. 960 (Oct. 17) 1914.
2. Lancet, p. 969 (Oct. 17) 1914.
3. Sou. Med. Jour., 7:30, 1914.

Book Reviews

Operative Orthopedics. By Willis C. Campbell, M.D., Memphis, Tennessee. 1154 pages, illustrated. St. Louis: The C. V. Mosby Company, 1939. Cloth $12.50.

This book is very complete. The author has not intended it to be an encyclopedia; however, it is an encyclopedia of the best operative orthopedics. As the author says: "Although many orthopedic affections are best treated by surgery alone, the majority are successfully treated by more conservative means." He does not wish to convey the impression that the most important methods of treatment are surgical.

Except for the chapters on arthroplasty and arthrodesis, operations are grouped according to their applicability to a given affection. This is an excellent arrangement, because less repetition as to generalities of etiology, pathology and treatment are involved than would be necessary in a classification made according to anatomic location. The chapter on arthroplasty, as one would expect, is one of the best written on the subject. The chapter on physiology emphasizes its importance of the subject. One of the best chapters is that on surgical approaches. Apparatus necessary in the treatment of orthopedic conditions is well described as are the foundations of surgical technic. The illustrations are detailed and excellent.

The book fulfills the current need and demand for a comprehensive work on operative orthopedics for the orthopedist and for those industrial and general surgeons who are doing good work in this branch of practice.

Functional Disorders of the Foot: Their Diagnosis and Treatment. By Frank D. Dickson, M.D., F.A.C.S., Orthopedic Surgeon, St. Luke's, Kansas City General and Wheatley Hospitals, Kansas City, Missouri, and Rex L. Diveley, A.B., M.D., F.A.C.S., Orthopedic Surgeon, St. Luke's, Kansas City General, Research and Wheatley Hospitals, Kansas City, Missouri. 305 pages, illustrated. Philadelphia: J. B. Lippincott Company, 1939. Cloth $5.00.

Written by two practical orthopedic surgeons and excellently illustrated, this book covers faulty foot balance and its correction at all ages. Just enough of the developmental background of the human foot is included to help one understand normal anatomy and physiology. Technic, where surgery is indicated, is thoroughly detailed. Corrective shoes and other useful appliances are adequately described.

This book is recommended as the most practical work on the foot that has been published to date in this country.

Medical Microbiology. By Kenneth L. Burdon, Ph.B., Sc.M., Ph.D., Assistant Professor of Immunology and Bacteriology, Louisiana State University School of Medicine, New Orleans. 763 pages, illustrated. New York: The Macmillan Company, 1939. Cloth $4.50.

Subjects of medical interest are discussed in this textbook under the usual bacteriologic classifications.

The handling of the microscope and bacteriologic technic are given. Infection and resistance, immunity, vaccines, serum and anaphylaxis are discussed.

In part four special attention is given to pathogenic

micro-organisms according to the system affected, as skin, mouth, throat, respiratory tract, and so on. There are special chapters on diphtheria, pneumonia, typhoid and tuberculosis. Infections acquired from animals, virus diseases, fungous infections, amebiasis and malaria are considered in the closing chapters.

Five appendices give information on metrology, thermometry, formulae and methods for preparation of culture media, reagents, stains, technic of biochemical tests, methods for standardization of antitoxins, the Wassermann, Kahn and Kline tests, certain immune reactions, including agglutinations, precipitin tests and blood matching and classified references. Review questions for each chapter are presented.

The text is illustrated by simple diagrams and occasional photographs. The book is brief, but comprehensive.

Public Health Law. By James A. Tobey, Dr.P.H., LL.D., Member of the New York Bar; Lecturer on Public Health Law at Harvard University School of Public Health and at Massachusetts Institute of Technology. Second Edition. 414 pages. New York: The Commonwealth Fund, 1939. Cloth $3.50.

"The condition of perfect health requires such laws and regulations as will secure to man associated in society the same sanitary enjoyments that he would have as an individual."

This book deals with principles and history of health legislation; also the sources of public health law, the police power, state health organizations and local health departments, and public health administration and liability.

It discusses the preparation and adoption of health legislation, law enforcement and court procedure. If public health laws are to stand the test of court analysis and are to advance the cause of public health, they must be written by informed persons.

Dr. Tobey brings out the limitations to law-making and rule-making. Health officers and others interested in public health legislation will profit by reading this book and keeping it at hand.

Beesly and Johnston's Manual of Surgical Anatomy. Revised by John Bruce, M.B., F.R.C.S. (Edin.), Assistant Surgeon, Edinburgh Royal Infirmary, and Robert Walmsley, M.D., Lecturer on Anatomy, University of Edinburgh. Fifth Edition. 733 pages, illustrated. New York: Oxford University Press, 1939. Cloth $5.50.

This short, thick handbook has been enlarged and thoroughly revised. It is a compact, tersely worded anatomy, made more readable by incorporation of numerous surgical considerations, as the subject matter unfolds. There are many excellent anatomical drawings and a few x-ray photographs throughout the book, although these seem somewhat insufficient for the clearest presentation of a very technical subject. The B.N.A. terminology is generally used. Due to the limitation in size of the volume, the delightful, concise and inclusive narrative suffers by the employment of a rather small type for the printing.

The Art of Anaesthesia. By Paluel J. Flagg, M.D., Visiting Anaesthetist to Manhattan Eye and Ear Hospital, New York City. Sixth Edition. 491 pages, illustrated. Philadelphia: J. B. Lippincott Company, 1939.

The author has brought up to date his extensive studies on asphyxia. The chapter on basal anesthesia has been enlarged. The various table positions in surgical practice have been revised. Special reference is made to methods of anesthesia for brain surgery and for thoracic surgery. The more recent gaseous agents for anesthesia and therapy are included.

An introductory chapter on the history of anesthesia is enjoyable and illuminating. Ether, the most widely used anesthetic, is taken as a basis for a broad and systematic presentation of inhalation anesthesias.

The discussion of local, regional and spinal anesthesia is purposely and disappointingly limited. Very little data are given on intravenous anesthesia, and sodium ethyl thiobarbiturate is not mentioned. There is no exposition of methods for grounding the apparatus in which inflammatory gases are used.

Other than the above exceptions, this volume is a clear-cut, readable, inclusive, well illustrated and scientific treatise on the art of anesthesia.

Roentgen Technic. By Clyde McNeill, M.D. 315 pages, illustrated. Springfield, Illinois: Charles C. Thomas, 1939. Cloth $5.00.

This book is divided into four sections, namely: the head; extremities; trunk; and exposure technic. Under the first three divisions the various positions are illustrated and described in detail; and accompanying each illustration is a drawing describing what should be shown in the films. Some of the illustrations have the actual reproduction of x-ray films. The author shows his own positions and those of other recognized authorities. Under the chapter "Exposure Technic" all the physical qualities of x-ray technic are discussed.

This book can be recommended as a good reference for technicians.

The Biology of Pneumococcus: The Bacteriological, Biochemical, and Immunological Characters and Activities of Diplococcus Pneumoniae. By Benjamin White, Ph.D., with the collaboration of Elliott Stirling Robinson, M.D., Ph.D., and Laverne Almon Barnes, Ph.D. 799 pages. New York: The Commonwealth Fund, 1938. Cloth $4.50.

A volume of 664 pages devoted to the study of a single bacterial organism must seem at first sight so truly formidable that the reader attacks the book with a feeling of desperate resolve and a brooding expectation of intellectual defeat. So much the greater is his enjoyment when he discovers that in this particular monograph the usually perfunctory opening chapter on history is readable and in fact interesting, that the succeeding chapters on general biology maintain and extend this interest and that the chapters on classification, on dissociation and the transformation and on chemical constituents not only hold the attention but create an ab-

sorbing interest in the fascinating story of the gradual unravelling of at least a part of "the riddles presented by this amazing bacterial cell." Nowhere can one get so intimate a picture of the tireless persistence of the scientific worker as in the story of the search by Avery and Dubos for an enzyme capable of splitting the polysaccharide of the pneumococcus capsule, the search that ended triumphantly in a cranberry bog.

Written by the late Dr. Benjamin White, the book purports to be no more than a review of the literature dealing with pneumococcus. It forms "a part of the pneumonia study and service carried on during the years 1931 to 1935 by the Massachusetts Department of Public Health under a grant from the Commonwealth Fund." But behind this modest statement of its origin and sponsorship lies a scholarship whose breadth may be gauged by the imposing list of articles and books included in its bibliography, a list that comprises 1593 references.

The authors' style is remarkable for its lucidity and the objective viewpoint is maintained with proper consistency. The monograph is, in short, a scientific achievement that demands first place as a source book and summary of our present day knowledge in its particular field. On the practical or applied side, there are highly instructive chapters on the treatment of pneumococcal infection and a final chapter charts the unsolved problems that lie ahead. An Appendix details the technical methods followed in the laboratory study of pneumococcus and in the preparation and standardization of antipneumococcic serum.

Study Guide Textbook in Anatomy and Physiology. By Carolyn E. Gray, A.M., R.N., and Caroline E. Stackpole, A.M., Associate in Biology, Teachers College, Columbia University. Fourth Edition. 105 pages, illustrated. New York: The Macmillan Company, 1939.

This book serves as a method of conducting quizzes in the study of anatomy. It contains 105 pages of practical tests and is based on "The Textbook of Anatomy and Physiology" by Kimber, Gray and Stackpole. The use of this book enables the teacher to rate the student's knowledge with greater accuracy and offers the student an excellent review.

Southern Medical News

OKLAHOMA CITY CLINICAL SOCIETY

The Oklahoma City Clinical Society, "to promote learning and fellowship among the medical profession of the great Southwest and to make available to it the educational advantages of the clinical material of Oklahoma City," will hold its seventh annual fall clinical conference at Oklahoma City at the Biltmore Hotel October 30, 31 and November 1-2. In this postgraduate assembly there will be sixteen guest lecturers, recognized leaders in their respective fields of practice, and in addition there will be seventy-two lecturers selected from the members of the Society in Oklahoma City, all having teaching ability and practical experience in the subject they will present. In addition to the lectures there will be round table luncheons and scientific and commercial exhibits. A registration fee of $10.00 covers all features of the assembly. Officers are: Dr. H. Dale Collins, President; Dr. Wendell Long, Director of Clinics; Dr. Basil A. Hayes, Vice-President; Dr. W. F. Keller, Secretary; and Dr. J. H. Robinson, Treasurer. Executive Committee: Dr. Ray M. Balyeat, Dr. Henry H. Turner, Dr. Philip M. McNeill, Dr. Earl D. McBride, Dr. J. C. MacDonald and Dr. Rex Bolend.

RADIOLOGICAL SOCIETY OF NORTH AMERICA

The twenty-fifth annual meeting of the Radiological Society of North America will be held at the Atlanta Biltmore Hotel in Atlanta, Georgia, December 10-15. Members of the medical associations are invited to attend. There is no registration fee. Program will consist of papers covering diagnosis and roentgenology, roentgen and radium therapy. Dr. James J. Clark, Atlanta, is Vice-President of the Radiological Society and General Chairman for the Atlanta meeting.

ALABAMA

The Jefferson County Medical Society held a postgraduate seminar in Birmingham on September 8 and 9 with the following doctors appearing on the program: Dr. Benjamin S. Barringer, New York; Dr. Hobart A. Reiman, Philadelphia; Dr. Angus M. McBryde, Durham, North Carolina; Dr. William F. Rienhoff, Baltimore; Dr. E. L. Sevringhaus, Madison, Wisconsin; and Dr. E. F. Traub, New York.

Dr. Herbert A. McClure, Butler, formerly Health Officer of Choctaw County, has been appointed Health Officer of Lamar County with headquarters in Vernon.

Dr. Robert K. Wilson, Dothan, has recently been appointed Health Officer of Pickens County to succeed Dr. Horace C. Hunt, Livingston, who has resigned to enter private practice.

Dr. David B. Snelling, Tuscumbia, has been appointed Health Officer of Choctaw County.

At a recent meeting of the Alabama Association of Railroad and Industrial Surgeons held at the Thomas Jefferson Hotel in Birmingham the following officers were elected for the coming year: President, Dr. C. N. Carraway, Birmingham; Vice-President, Dr. N. S. Johnson, Clanton; Secretary, Dr. J. U. Ray, Woodstock, reelected.

Dr. William Clegg Eversole, Vincent, and Miss Vivian Duncan Booker, Birmingham, were recently married.

Dr. George Sellers Graham, Birmingham, and Dr. Sarah Henrietta McCarty, Edinburgh, Scotland, were married July 12.

Dr. James Gibson Smith, Birmingham, and Miss Ruth Niskern, St. Cloud, Minnesota, were married in June.

DEATHS

Dr. C. C. Jones, Birmingham, aged 93, died September 7 of senility.

Dr. Dewitt C. Walker, Decatur, aged 62, died September 8 after a heart attack.

Dr. John Forney Rowan, Jacksonville, aged 81, died May 12.

Dr. Hosea Franklin Downs, Clanton, aged 50, died May 9 of pulmonary tuberculosis.

ARKANSAS

Dr. J. K. Donaldson, Little Rock, State Director of the Committee on Publicity on Appendiceal Disease, Section on Surgery, Southern Medical Association, has appointed the following Central Advisory Committee: Dr. A. S. Buchanan, Prescott; Dr. W. R. Brooksher, Fort Smith; Dr. F. A. Corn, Lonoke; Dr. S. P. Cromer, Little Rock; Dr. W. B. Grayson, Little Rock; Dr. H. T. Smith, McGehee; Dr. S. J. Wolfermann, Fort Smith; and Dr. W. T. Wootton, Hot Springs National Park.

Dr. Ellery C. Gay, Little Rock, has recently been appointed Medical Supervisor of the Crippled Children's Division of the State Department of Public Welfare, succeeding Dr. Lee Vallette Parmley, resigned.

Dr. Donald W. Dykstra, Morrilton, has recently been appointed in charge of the new Syphilis Control Division of the State Department of Health.

Dr. James W. Branch, Hope, did graduate work at the Cook County Hospital in Chicago during the month of August.

Dr. Fount Richardson, Fayetteville, has been appointed Major in the Medical Corps of the Arkansas National Guard.

Dr. C. E. Arkebauer, Little Rock, recently completed his thirty-eighth year of service with the State Hospital.

Dr. W. M. Woods, Huntington, and Miss Mary Seawell, Muskogee, Oklahoma, were married July 2.

DEATHS

Dr. George Thomas Laman, Cave City, aged 60, died August 8.

Continued on page 34

DOCTOR! *You are invited to attend . . .*

THE OKLAHOMA CITY CLINICAL SOCIETY'S
NINTH ANNUAL FALL CLINICAL CONFERENCE

October 30, 31, November 1, 2, 1939

——— Sixteen Distinguished Guest Lecturers ———

DR. ALBERT H. ALDRIDGE, Obstetrics, New York; Clinc. Prof. Obs. and Gyn., Columbia University; Chief Surg., Woman's Hospital, New York.

DR. EDGAR G. BALLENGER, Urology, Atlanta; Urologist, Crawford W. Long Memorial Hosp.; Consulting Urologist, Henry Grady Memorial Hosp.; Pres. Amer. Urological Association.

DR. LEWELLYS F. BARKER, Internal Med., Baltimore; Prof. Emeritus of Med., Johns Hopkins U.; Visiting Phys., Johns Hopkins Hospital.

DR. LOWELL S. GOIN, Roentgenology, Los Angeles; Consulting Radiologist, Los Angeles Board of Education; Radiologist, L. A. Orthopedic Hosp., Radiologist and Chairman of Exec. Board Queen of Angels Hosp.

DR. HARRY S. GRADLE, Ophthalmology, Chicago; Extramural Prof., Northwestern U.; Chief of Staff, Ill. Eye and Ear Infir.; Attending Oph. at Michael Reese Hosp., Chicago.

DR. JOHN A. KOLMER, Pathology, Philadelphia; Prof. of Med. Temple U.; Director of Research Institute of Cutaneous Med.; Physician to Temple U. Hosp.

DR. FRANK H. LAHEY, Surgery, Boston; Director of Lahey Clinic, Boston; Surgeon-in-chief, New Eng. Baptist Hosp.; Surgeon-in-chief, New Eng. Deaconess Hosp.

DR. JOE V. MEIGS, Gynecology, Boston; Instr. in Surg., Harvard Med. School; Visiting Surg., Mass. Gen. Hosp.; Surgeon, Pondville Hosp., Mass. Dept. Public Health.

DR. A. GRAEME MITCHELL, Pediatrics, Cincinnati; Prof. of Ped., Univ. of Cincinnati Col. of Med.; Director and Chief of Staff, Children's Hosp., Cincinnati.

DR. EMIL NOVAK, Endocrinology-Gynecology, Baltimore; Assoc. Prof. Gynecology, Johns Hopkins Med. Col.; Visiting Gyn., Bon Secours and St. Agnes Hosp.

DR. HOBART A. REIMANN, Internal Medicine, Philadelphia; Prof. of Med., Jefferson Med. College; Attending Physician, Jefferson Hospital.

DR. ERWIN R. SCHMIDT, Surgery, Madison; Prof. of Surg., Univ. of Wisconsin Med. School; Chief Surg., State of Wisconsin Gen. Hospital.

DR. HERMAN C. SCHUMM, Orthopedics, Milwaukee; Clin. Prof. and Director of Division of Orthopedic Surg., Marquette Univ.; Assoc. Prof. of Orthopedic Surg., Univ. of Wis.

DR. ROCK SLEYSTER, Psychiatry, Wauwatosa, Wis.; Board of Trustees, Marquette Univ.; Medical Director, Milwaukee Sanitarium; President of American Medical Association.

DR. MARION B. SULZBERGER, Dermatology, New York; Asst. Clin. Prof. of Der. and Syph., Skin and Cancer Unit of N. Y. PG Med. School and Hosp. of Columbia Univ.

DR. WILLIAM A. WAGNER, Otolaryngology, New Orleans; Asst. Prof. Otolaryn., Tulane Univ. School of Med.; Visiting Surg., Charity Hosp.; Visiting Surg., Eye, Ear, Nose and Throat Hosp.

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DEPARTMENT OF GRADUATE MEDICAL STUDIES
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Continued from page 1076

Dr. Jacob H. C. King, Hot Springs National Park, aged 78, died June 5.

Dr. Monroe Patterson, Eudora, aged 53, died June 11.

Dr. W. S. Davis, Owensville, aged 83, died June 13.

Dr. William V. Laws, Hot Springs National Park, aged 73, died June 9 of chronic myocarditis and nephritis.

Dr. Ernest M. Thompson, Fayetteville, aged 68, died May 28 of chronic myocarditis.

DISTRICT OF COLUMBIA

Dr. Charles Stanley White, President of the Doctors' Hospital, presided recently at the ceremony for the laying of the cornerstone for the new Doctors' Hospital, which is adjacent to the Washington Medical Building. Dr. White handled the trowel for the laying of the cornerstone. Dr. Oscar B. Hunter placed a large metal cylinder within the cornerstone containing the usual articles and various records pertaining to the organization and construction of the Doctors' Hospital.

Dr. John W. Warner, Washington, has been appointed Chairman of the Doctors' Division of the District of Columbia Chapter of the American Red Cross.

Dr. LeRoy M. Robins, Washington, and Miss Naomi Ellisberg, Raleigh, North Carolina, were married June 24.

DEATHS

Dr. Everett Monroe Ellison, Washington, aged 60, died July 24 from a heart attack.

Dr. Charles Edward Holton, Washington, aged 70, died May 22.

Dr. Roy Richard Jones, Washington, aged 48, died June 13 of complications following an operation for appendicitis.

Dr. Bittle Cornelius Keister, Washington, aged 82, died May 3.

FLORIDA

Dr. Albert B. McCreary, Jacksonville, has been appointed State Health Officer to succeed the late Dr. Wilbur A. McPhaul.

Continued on page 35

THE NEW YORK POLYCLINIC

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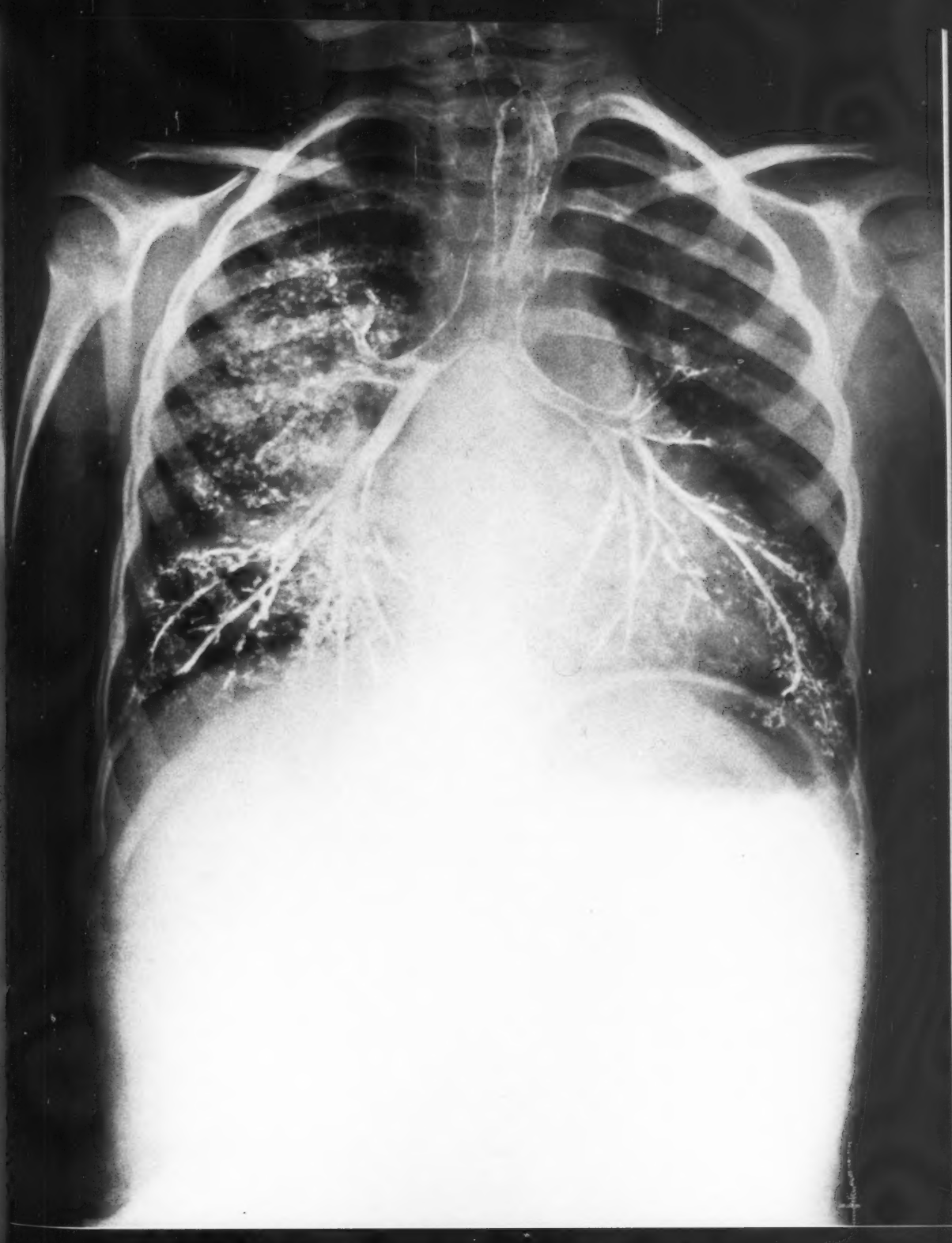

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Excerpt from the Medical Literature....

"Chronic pulmonary lesions probably offer the most important indications for roentgen examinations for differential diagnosis. Chronic bronchitis, bronchial asthma, emphysema, bronchial stenosis, bronchiectasis, pneumoconiosis, pulmonary congestion, pulmonary tuberculosis, syphilis, mycotic infections, lung tumors, and pleuritic lesions, as isolated or co-existing conditions, may all present similar symptoms and signs which may render their clinical recognition difficult or impossible. In some of them the roentgen examination adds little to the clinical diagnosis other than to rule out the presence of associated lesions. In most of them, however, it presents conclusive evidence which may confirm or establish the diagnosis."

—Illinois M. J., *74*:245, September, 1938.

The obvious excellence of the original radiograph reproduced on the reverse side of this page is due, first, to the knowledge of the radiologist; second, to the inherent qualities of Eastman Ultra-Speed X-ray Film.

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(*See reverse side of this page*)

Continued from page 34

Dr. George R. Creekmore, Brooksville, has been made a member of the Board of Commissioners of Hernando County.

Dr. L. C. Gonzalez, Jacksonville, will spend the coming year at Johns Hopkins University taking a postgraduate course in venereal disease control.

Dr. B. B. Sory, Jr., Palm Beach, is now vacationing in Paris, France, prior to taking advanced medical study in Vienna, Austria.

Dr. Maurice E. Heck, Miami, did special work in surgery and gynecology at Chicago and Mayo Clinic during the month of August.

Dr. M. A. Lischoff, Pensacola, spent the month of August in Philadelphia doing special work in broncho-esophagoscopy.

Dr. Robert P. Keiser, Miami, and Miss Alice Bidlingmaier, Hollywood, were married July 1.

Dr. R. L. Laymon, Miami, and Miss Marjorie Rich, Washington, D. C., were married July 7.

Dr. R. Spencer Howell, Miami, and Miss Mary Louise Mullino, Montezuma, Georgia, were married June 7.

DEATHS

Dr. Wilbur A. McPhaul, Jacksonville, aged 60, died August 1 following an illness of several months.

Dr. John T. Denton, Sanford, aged 60, died August 3 in a hospital at Greenville, South Carolina, following a sudden illness suffered while attending the Southern Pediatric Seminar at Saluda.

Dr. Gaston Day, Jacksonville, aged 57, died August 5.

Dr. Isaac H. Springer, Daytona Beach, aged 85, died May 31 of cerebral hemorrhage.

Dr. Louis George Corbett, Tampa, aged 83, died June 17 of carcinoma of the stomach.

GEORGIA

In an expanded health program the State Department of Health has established six regional Health Units under the supervision of the following Regional Medical Directors: Dr. Bert H. Malone, Southeastern District with headquarters at Waycross; Dr. Robert B. Griffin, Northwestern District with headquarters at Marietta; Dr. Aaron Wilson Brown, Northeastern District with headquarters at Gainesville; Dr. Rufus Floyd Payne, West Central District with headquarters at Griffin; Dr. John M. Walton, East Central District with headquarters at Swainsboro; Dr. Lester M. Petrie, Southwestern District with headquarters at Albany.

Dr. Richard C. Shepard, Lafayette, has entered private practice and resigned as Health Commissioner of Walker and Catoosa Counties.

Dr. Stuart P. Vandiviere, formerly of Franklin, North Carolina, has been placed in charge of the Baldwin County Health Department.

Dr. Anthony H. Gallis and Miss Frances Skundale, both of Atlanta, were married June 11.

Dr. Williams Dean Steward, Augusta, and Miss Martha Frances Boyd, Chattanooga, Tennessee, were married in June.

DEATHS

Dr. Francis Edwin Van der Veer, Atlanta, aged 66, died May 30 of cerebral hemorrhage.

Dr. Isadore J. Pass, Macon, aged 30, died June 9 of injuries received in an automobile accident.

Dr. Henry Homer Jones, Coolidge, aged 69, died July 8.

Dr. William H. Whitehead, Austell, aged 83, died July 10.

Dr. Tully M. Talbot, Valdosta, aged 80, died July 9.

Dr. Harvey Dorman Kemper, Jonesboro, aged 60, died July 14.

Dr. Newton Jasper Coker, Canton, aged 71, died September 12.

KENTUCKY

The Southern Psychiatric Association will hold its fifth annual meeting at the Brown Hotel, Louisville, October 9 and 10.

Dr. John W. Fish, Louisville, has opened offices in the Brown Building, with practice limited to diseases of the eye.

Dr. Hugh R. Leavell, Louisville, has returned to resume his duties as Health Officer after a year's study at Yale University, where he received the degree of Doctor of Public Health.

Dr. Ralph C. Lake, Georgetown, and Miss Frances Blanche Binford, Springfield, were married July 5.

Continued on page 36

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Continued from page 35

DEATHS

Dr. Fred Gordon La Rue, Lexington, aged 72, died May 25 of hypostatic pneumonia and hypertensive heart disease.

Dr. James Jackson Backus, Gracey, aged 82, died June 23 of coronary thrombosis.

Dr. John L. Seay, Eastwood, aged 71, died May 29 of injuries received when struck by an automobile.

Dr. Feodor W. Koehler, Louisville, aged 82, died May 30 of coronary occlusion.

Dr. Claude Graham Hoffman, Louisville, aged 50, died June 24 of cerebral hemorrhage.

Dr. Thomas H. Kinnaird, Lexington, aged 84, died June 25 of chronic pyelonephritis.

Dr. W. P. Roberts, Lexington, aged 70, died June 19 of arteriosclerotic heart disease.

LOUISIANA

Dr. Joseph Rigney D'Aunoy, New Orleans, Dean and Professor of Pathology and Bacteriology, Louisiana State University Medical Center, has been decorated with the Order of Commendatore of the Crown of Italy "in recognition of his achievements in the fields of medical research and education."

Dr. Nathan H. Polmer, Director, Division of Physical Therapy, Graduate School of Medicine, Louisiana State University, was named President-Elect of the American Congress of Physical Therapy at the recent annual meeting in New York.

Dr. Roy W. Wright, New Orleans, has been appointed Director of Charity Hospital.

Dr. Thomas C. Paulsen, Baton Rouge, has recently been appointed physician to the Louisiana State University and Medical Director of its hospital.

Dr. Ambrose H. Storck, New Orleans, has returned after visiting surgical clinics in England, Scotland, the Scandinavian states and the Continent.

Dr. J. D. Rives, New Orleans, Chairman for the Louisiana Division of the Committee on Publicity on Appendiceal Disease, Section on Surgery, Southern Medical Association, has the following members on his Committee: Dr. Ambrose H. Storck, New Orleans; Dr. Charles McVea, Baton Rouge; Dr. A. L. Culpepper, Alexandria; Dr. George W. Wright, Monroe; Dr. Paul D. Abramson, Shreveport; and Dr. Walter Moss, Lake Charles.

DEATHS

Dr. Orin Eastland, Shreveport, aged 81, died June 10 of pyelonephritis.

Dr. Dixie Navarro Foster, Franklin, aged 76, died June 15 of cerebral hemorrhage.

Dr. Jackson J. Ayo, Raceland, aged 70, died August 17 after a prolonged illness.

Dr. George R. Beridon, Opelousas, aged 48, died July 28.

MARYLAND

The Rockefeller Foundation has awarded two grants to Johns Hopkins University School of Medicine, Baltimore, $350,000 to be used over a ten-year period to equip and maintain a Department of Preventive Medicine and $90,000 to be used as a research fund to be distributed among departments and to projects which stand in greatest need.

Dr. Robert H. Riley, Baltimore, was recently given a testimonial banquet in celebration of having served twenty-five years on the staff of the State Health Department.

Dr. Frank B. Hines, Chestertown, has been appointed Deputy Medical Examiner for Kent County by the Maryland Postmortem Examiners' Commission.

Dr. John Rathbone Oliver, Baltimore, Associate in the History of Medicine at Johns Hopkins University School of Medicine, has announced his retirement.

Dr. James Marshall Hanna Rowland, Baltimore, has retired as Dean of the University of Maryland School of Medicine.

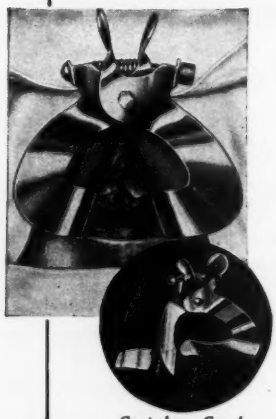
Dr. J. Winthrop Peabody, Glenn Dale, has resigned his post as General Superintendent of the Tuberculosis Sanatoria and his former assistant, Dr. Daniel Leo Finucane, will succeed him.

DEATHS

Dr. Henry H. Brundage, Bethesda, aged 79, died May 5 of carcinoma of the stomach.

Dr. Columbus C. Ward, Crisfield, aged 74, died May 26 of carcinoma of the pancreas.

Continued on page 38



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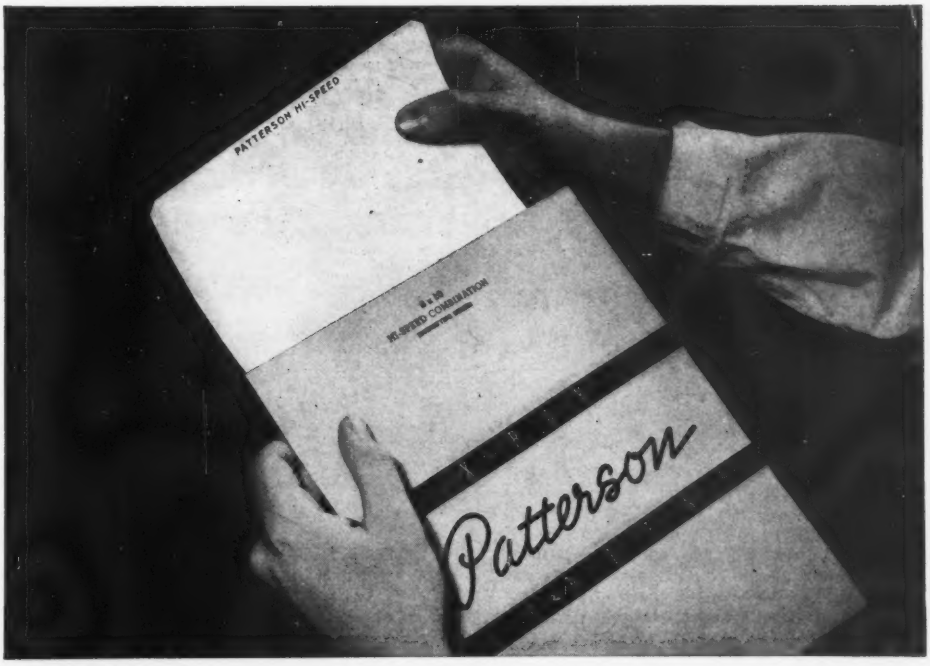

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*Archives of Pediatrics, 54:533-547, Sept., 1937

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Continued from page 36

Dr. Edward Engler Gibbons, Baltimore, aged 67, died May 30 of acute myocarditis.

Dr. Otto Wolfgang Wichelhausen, Baltimore, aged 35, died August 14.

MISSISSIPPI

Dr. A. E. Thayer, Meridian, announces the opening of a laboratory in the Threefoot Building for the exclusive study and diagnosis of surgical tissues.

Dr. Gilruth Darrington, Yazoo City, is President of the Mississippi State Hospital Association.

Dr. J. A. Milne, Director of County Health Work, has announced the new health officer trainees in the state are as follows: Dr. Everett W. Ryan, Ambrosia, Missouri; Dr. Robert Henry Bostwick, Jr., Indianola, Mississippi; Dr. Raymond F. Mayer, Pomaria, South Carolina.

Dr. Charles V. Akin, formerly of Meridian, has been appointed Assistant Surgeon General of the United States Public Health Service in charge of the Division of Sanitation Reports and Statistics.

DEATHS

Dr. Joseph Thomas Ware, Starkville, aged 70, died May 4.

Dr. John Duncan Smith, Laurel, aged 66, died in May of heart disease.

MISSOURI

Dr. Robert A. Moore, formerly connected with Cornell University Medical College, New York, has recently been appointed Edward Mallinckrodt Professor of Pathology at Washington University School of Medicine, St. Louis.

Dr. Frank C. Nifong, Columbia, was recently honored by a barbecue held by the Boone County Medical Society marking his retirement after fifty years in the practice of medicine. He was presented with a medallion.

Dr. M. B. Clopton, St. Louis, President of the State Board of Health, was master of ceremonies for the laying of the cornerstone of the new Missouri Trachoma Hospital at Rolla.

The Annual Fall Clinical Conference of the Kansas City Southwest Clinical Society will be held in Kansas City on October 2-5.

DEATHS

Dr. Claude G. Martin, Joplin, aged 56, died May 22 of coronary heart disease.

Dr. John Jacob Osterhout, Belleview, aged 62, died June 4 of coronary sclerosis.

Dr. Edward Schulz, St. Louis, aged 68, died June 28 of carcinoma.

Dr. Ewing S. Moad, Blue Springs, aged 79, died June 21 of chronic nephritis and endarteritis obliterans.

Dr. John A. Van Amburg, Lutesville, aged 78, died June 15 of chronic cholecystitis.

Dr. Clyde Clifford Winter, Farmington, aged 60, died June 30.

Dr. Henry Tipton Byars, Caruthersville, aged 79, died June 5.

Dr. Aaron Levy, St. Louis, aged 63, died June 18.

Dr. C. T. Hackleman, Pleasant View, aged 88, died May 17.

Dr. Harry Alexander Simrell, Stockton, aged 52, died May 22 of meningoencephalitis.

NORTH CAROLINA

Dr. Paul H. Ringer, Asheville, was recently elected Vice-President of the National Tuberculosis Association at the annual meeting in Boston, Massachusetts.

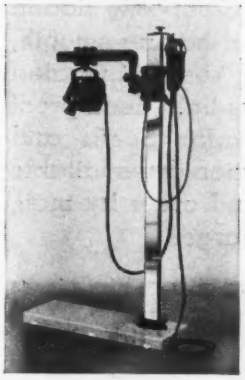
Wake Forest College School of Medical Sciences, Wake Forest, is to be moved to Winston-Salem and expanded into a four-year school with a capacity for two hundred students. Hospital facilities will be provided by the North Carolina Baptist Hospital. Funds have been provided by the Bowman Gray Fund from the estate of the late Mr. Gray, a tobacco magnate of Winston-Salem.

The Asheville Orthopedic Home for convalescent orthopedic patients was recently dedicated. This enterprise is sponsored by the Rotary Club of Asheville and the Asheville Junior League. Dr. John T. Saunders, Asheville, is the orthopedic surgeon in charge of the home.

A bronze bust of Dr. LeGrand Guerry, Columbia, was presented to Columbia Hospital by a group of friends and former patients.

Dr. Frederick R. Taylor, High Point, has recently been elected

Continued on page 40



HERE'S a mobile-portable x-ray unit that's so compact it can be packed in two attractive cases; so light-weight and easy-to-carry that a single trip takes the whole outfit from office to car! It's the unique G-E Model F-3-35 which combines the popular Model F-3 portable x-ray unit with the new Model 35 mobile-portable tube stand.

All around it's an ideal unit for the medical man who does not have adequate roentgenological service readily available. It provides flexibility and accurate adjustment in a thoroughly practical office-mobile unit that can be "knocked down," packed up, and immediately converted to a portable unit without limiting its flexibility or wide range of service.

Packed in their cases the units balance each other and are easy to carry.

For portable service the carrying case cover serves as a base; eliminates need of carrying mobile base on calls.

To best evaluate this fine unit, see it yourself. We will be glad to arrange an interesting working demonstration for you, in your office, at your convenience. Just check, sign, and mail the handy coupon, today.

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NAME .....

ADDRESS ..... CITY .....

A310

Continued from page 38

to alumni membership in the Haverford College Chapter of Phi Beta Kappa.

Dr. David G. Welton, formerly instructor in Dermatology at the University of Michigan Medical School, is now associated with Dr. Joseph A. Elliott, Charlotte.

Dr. Laurie R. Teasdale, Charlotte, has opened offices at 117 West Seventh Street for the practice of otolaryngology and peroral endoscopy.

Dr. Charles Burdis Davis, Jr., and Miss Margaret MacRae Williams, both of Wilmington, were married July 15.

Dr. David William Martin, Durham, and Miss Joanna Ward Law, Austin, Texas, were married June 23.

Dr. Jefferson Davis, Waxhaw, and Miss Frances Evelyn Little, Statesville, were married July 15.

Dr. D. Forest Moore, Shelby, and Miss Eleanor Lyon, Terrell, were married July 26.

Dr. Robert Monroe McMillan, Candor, and Miss Dorothy Burchfield, Danville, Pennsylvania, were married July 12.

Deaths

Dr. Jacob Franklin Highsmith, Fayetteville, aged 70, died June 22 of cerebral and coronary embolism.

Dr. Isaac W. Lamm, Lucama, aged 74, died June 20 of coronary occlusion.

Dr. Horace N. Abernethy, Charlotte, aged 74, died June 10 of cerebral hemorrhage.

Dr. Thomas Sampson Royster, Henderson, aged 49, died August 1 of a cardiac disease.

Dr. Henry Fletcher Long, Statesville, aged 70, died July 28.

Dr. James Bryant Person, Selma, aged 66, died July 16.

Dr. W. O. House, Harboro, aged 46, was killed in an airplane accident August 22.

OKLAHOMA

Dr. Henry H. Turner, Oklahoma City, is to be Associate Professor of Medicine, and Dr. Ernest Lachmann, Oklahoma City, is to be Associate Professor of Anatomy, University of Oklahoma School of Medicine, according to an announcement by Dr. Robert U. Patterson, Dean.

Dr. Maynard S. Hart, Oklahoma City, has recently been named Assistant Director of the Laboratories at the University of Oklahoma and Crippled Children's Hospital.

Dr. Francis Polk Fry, Jr., Frederick, has been made Health Officer of Tillman County.

Dr. James C. Rumley, Stigler, has been made Health Officer of Haskell County.

Dr. John I. Derr, Waurika, has been made Health Officer of Jefferson County.

Dr. Simon S. Garrett, Duncan, has been made Health Officer of Stephens County.

Dr. Lloyd T. Lancaster, Cherokee, has been made Health Officer of Alfalfa County.

Dr. Loren V. Baker, Elk City, has been made Health Officer of Beckham County.

Dr. William F. Griffin, Watonga, has been made Health Officer of Blaine County.

Dr. Robert K. McIntosh, Jr., Tahlequah, has been made Health Officer of Cherokee County.

Dr. Joshua P. Beam, Arnett, has been made Health Officer of Ellis County.

Dr. William S. Cary, Reydon, has been made Health Officer of Roger Mills County.

Dr. Walter R. Joblin, Porter, has been made Health Officer of Wagner County.

Dr. Hugh H. Monroe, Lindsay, has been made Health Officer of Garvin County.

Dr. Ferdinand R. Hassler, Jr., Seminole, has been made Health Officer of Pottawatomie County.

Deaths

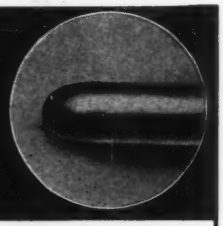
Dr. Floyd Jackson Bolend, Oklahoma City, aged 61, died June 22 of coronary thrombosis.

Dr. Eugene Orvin Barker, Guthrie, aged 84, died June 24 of coronary thrombosis.

Dr. John Franklin Rice, Vinita, aged 79, died May 23 of cerebral arteriosclerosis.

Continued on page 42

RADON SEEDS



FOR safety and reliability use composite Radon seeds in your cases requiring interstitial radiation. The Composite Radon Seed is the only type of metal Radon Seed having smooth, round, non-cutting ends. In this type of seed, illustrated here highly magnified, Radon is under gas-tight, leak-proof seal. Composite Platinum (or Gold) Radon Seeds and loading-slot instruments for their implantation are available to you exclusively through us. Inquire and order by mail, or preferably by telegraph, reversing charges.

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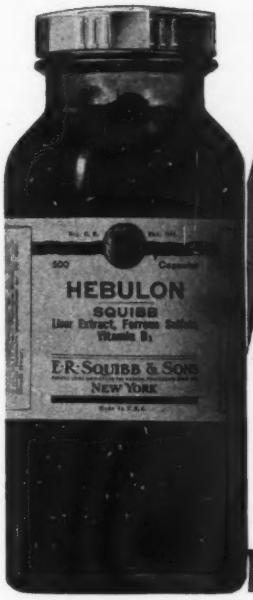

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Convenience—Hebulon* is a soft gelatin capsule—easily swallowed and free from objectionable odor. Dosage is easily regulated and discomfort of injections avoided.

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Liver Extract: 2 grains derived from 16 grams of fresh bovine liver.

Vitamin B_1: 25 International units of pure crystalline Vitamin B_1.

Vitamin B Complex Factors—also contains Riboflavin and the filtrate factor, present in the liver extract.

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Hebulon is indicated in the anemias and other conditions associated with iron deficiency, particularly in those patients in whom gastric function may be deficient and in whom the need of Vitamin B_1 seems apparent. Next time you have a case requiring iron, liver extract and Vitamin B_1, prescribe Hebulon Capsules. They are available in bottles of 100, 500 and 1000.

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Continued from page 40

SOUTH CAROLINA

Dr. Robert Wilson, Charleston, has been selected by the American Legion for their plaque for distinguished service to South Carolina.

Dr. Elliott Finger, Marion, has returned after doing postgraduate work in Chicago.

Dr. Frank C. Owens, Columbia, has been made Chairman of the Public Employees Division of the Columbia Community Chest.

Dr. Samuel Oliver Cantey, Jr., and Miss Elizabeth Yates Simmons, both of Charleston, were married June 14.

Dr. Alton Grady Brown, Rock Hill, and Miss Nellie Claire Sanders, Charleston, were married June 2.

Dr. John Pratt, Columbia, and Miss Helen Wells, Charleston, were married August 23.

Deaths

Dr. William J. Smith, Anderson, aged 60, died May 22.

Dr. William H. Kelly, Spartanburg, aged 77, died May 22.

Dr. John Alex Meldau, McClellanville, aged 80, died June 17 of cerebral hemorrhage.

TENNESSEE

Deaths

Dr. Charles Gaston Wilson, Clarksville, aged 79, died May 2 of influenza and pneumonia.

Dr. William M. Boyd, Madison, aged 79, died May 18 of fracture of the ribs resulting from a fall and pneumonia.

Dr. William H. Balthrop, Nashville, aged 88, died June 24 of cerebral hemorrhage.

Dr. Brainard B. Gracy, Smyrna, aged 89, died May 3 of prostatitis.

Dr. Lemuel B. McWhorter, Chattanooga, aged 77, died May 23.

Dr. James Richard Thompson, Manchester, aged 91, died June 12 as the result of injuries received in an automobile accident.

Dr. George W. Pearson, Manchester, aged 86, died June 8 of bacillary dysentery.

Dr. George Weldon Oliver, Medina, aged 70, died July 9.

Dr. J. R. Conyers, Gates, aged 77, died July 11.

Dr. W. J. Winters, Chattanooga, aged 66, died June 5.

TEXAS

Dr. James S. Sweeney, Dallas, recently received the honorary degree of Doctor of Laws from Texas Christian University at the commencement exercises.

Dr. James R. Barcus, Gladewater, has been appointed Health Officer of Gladewater.

Dr. Samuel C. Red, Houston, was recently honored by a dinner at the Houston Club given by the Harris County Medical Society and its Woman's Auxiliary commemorating his fifty-second year in the practice of medicine.

The recently organized Dallas Academy of Internal Medicine has elected the following officers: President, Dr. David W. Carter, Jr., Dallas; Vice-President, Dr. Walter G. Reddick, Dallas; Secretary, Dr. Edward S. Ross, Dallas.

Dr. H. Frank Carman, Dallas, was elected a member of the Executive Committee of the National Tuberculosis Association at the recent meeting in Boston, Massachusetts.

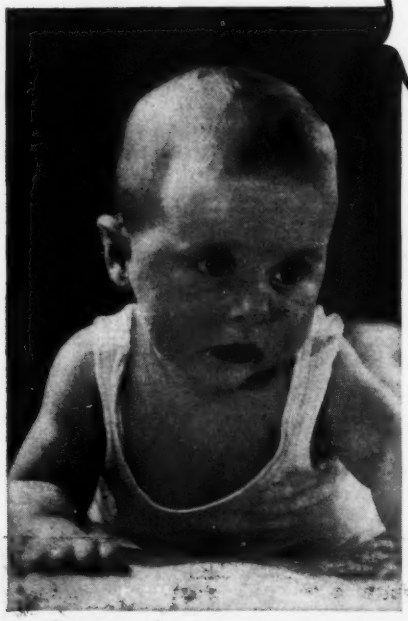
Dr. Oscar M. Marchman, Dallas, was recently elected a member of the Board of Managers of the American Society for the Hard of Hearing.

Dr. R. E. Cogswell, Dimmitt, has recently completed three months' postgraduate study at the Mayo Clinic, Rochester.

Dr. Minnie Maffett, Dallas, has been elected President of the National Federation of Business and Professional Women's Clubs at the recent meeting of the organization in Kansas City.

Dr. C. M. Kent, Kenedy, has purchased the interest of Dr. John W. Worsham in the Kenedy Clinic and Hospital.

Continued on page 44



WON'T YOU HELP ME KEEP MY DINNER DOWN?

TWO FREQUENT CAUSES of vomiting in artificially fed infants are excessive fat intake and inability to cope with large, tough milk curds.

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1. DRYCO modifications provide a *moderate* fat level, commensurate with the lessened tolerance of the average infant for cow's milk fat.
2. DRYCO modifications form no large, tough curds to retard digestion and induce vomiting. The protein of DRYCO forms a soft, flocculent coagulum in the infant's stomach.

DRYCO

THE OBSTINATE CASE

FOR those cases of constipation that resist the mild stimulation of Mucilose alone, such as are encountered in senility and in pregnancy, regulation can be accomplished with the most recent development in this field—

MUCILOSE GRANULES WITH KASAGRA

Containing approximately 55% Mucilose and 45% dextrose, with 4 minims of Kasagra to the teaspoonful, provides bland, smooth bulk and lubrication in addition to gentle laxative action. The active factors are:

1. Mucilose—a hemicellulose obtained from Plantago loeflingii. Well recognized in constipation and colitis management for its remarkable ability to swell in the presence of liquid and form a mucilaginous mass, which lubricates the mucosa without leakage and eases elimination.

2. Kasagra—a Stearns development. Each minim of Kasagra represents the gentle tonic laxative properties of one grain of cascara sagrada bark.

Dose: one to two teaspoonfuls, followed by copious water.

Mucilose Available in Three Forms

Mucilose Granules with Kasagra—in 4 oz. bottles
Mucilose Flakes, 4 oz. and 16 oz. bottles
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the Original Malted Milk
NOW AT NEW LOW PRICES

Continued from page 42

The members of the staff of St. Joseph's Hospital, Fort Worth, have elected the following officers: Chairman, Dr. Frank S. Schoonover; Vice-Chairman, Dr. F. L. Snyder; Secretary, Dr. Tom Bond.

The members of the staff of Wichita General Hospital, Wichita Falls, have elected the following officers: President, Dr. Carl E. Mangum; Vice-President, Dr. Fred R. Landon; Secretary, Dr. Otto C. Egdorf (reelected).

Dr. John G. Welch, Port Neches, has recently been made Health Officer of Beaumont.

Dr. Charles F. Hull, Carthage, has recently been appointed Health Officer of Panola County.

Dr. Nicholas E. Dobos, San Antonio, and Miss June R. McConnell, Greensburgh, Indiana, were married June 1.

Dr. Van C. Tipton, formerly of Austin, has been appointed Director of the San Antonio Health Department.

Dr. Ernest W. Prothro, Corpus Christi, has recently been appointed Health Officer of Nueces County and Corpus Christi.

Dr. Taylor C. Gilbert, Dallas, and Miss Edyth Erhard, Temple, were married recently.

Dr. Robert J. Rowe, Jr., Kaufman, and Miss Ruth Milner, Dallas, were married July 1.

Dr. Robert H. Brooks and Miss Martha Helen Waddle, both of Jacobia, were married June 23.

Dr. L. J. Alexander has moved from Dallas to Baltimore, Maryland.

Dr. J. B. Birt has moved from Harper to Sanatorium.

Dr. R. J. Brady has moved from Houston to Galveston.

Dr. Ruby K. Daniel has moved from Rochester, Minnesota, to Dallas.

Dr. A. M. Dashiell has moved from Bryan to Austin.

Dr. Gilbert B. Greene has moved from Robstown to Birmingham, Alabama.

Dr. Robert S. Hardwick has moved from El Paso to East Chicago, Indiana.

Dr. W. O. Hearn has moved from Enloe to Paris.

Dr. Charles M. Hoch has moved from Stamford to Bryson.

Dr. John J. Hopper has moved from Temple to Brownwood.

Dr. Robert R. Jones has moved from Terrell to Midland.

Dr. J. R. Maxfield, Jr., has moved from Dallas to San Francisco, California.

Dr. Ernest A. Maxwell has moved from Galveston to San Antonio.

Dr. I. Sellers Moore has moved from Midland to Kenedy.

Dr. T. L. Morgan has moved from Midland to Hobbs, New Mexico.

Dr. Ross Owens has moved from Dallas to Decatur.

Dr. C. C. Quillian has moved from Sugar Land to Kenedy.

Dr. V. S. Rabb has moved from Tyler to Austin.

Dr. T. P. Reeder has moved from Quanah to Newport Beach, California.

Dr. B. F. Roche has moved from Monahans to Bay City.

Dr. Van C. Tipton has moved from Austin to San Antonio.

Dr. Luther O. Whitman has moved from San Antonio to Port Aransas.

Dr. Luther L. Zarr has moved from Temple to Houston.

Deaths

Dr. Joseph H. Gandy, Lipan, aged 57, died May 18 of coronary occlusion.

Dr. Roy DeLisle Wilson, Houston, aged 53, died May 13.

Dr. Eugene Arthur Redlinger, Dallas, aged 67, died May 18 of coronary occlusion.

Dr. Thomas Owings Staples, Wylie, aged 78, died May 18 of cardiac asthma.

Dr. Edward C. Bechtol, Grapevine, aged 79, died June 20 of cerebral thrombosis.

Dr. Harlan Horney, San Angelo, aged 69, died June 21 of cerebral thrombosis.

Dr. Louis Goldstein, Beaumont, aged 77, died June 25 of bronchopneumonia.

Dr. Charles L. King, Whitesboro, aged 80, died June 14 of cerebral hemorrhage.

Dr. James Nathan Gee, Bethel, aged 72, died June 30 of coronary occlusion.

Dr. Thomas Richard Sealy, Santa Anna, aged 59, died June 15 of cirrhosis of the liver.

Dr. Thomas Richardson Morehead, Mertzon, aged 64, died June 2 of cerebral hemorrhage and hypertension.

Continued on page 46

Light area represents a day's energy output by a test subject during the training period before gelatine feedings were started. Dark area represents a day's energy output by the same subject after gelatine feedings. In both cases the subject worked to the point of exhaustion.

Muscular Energy Doubled

By PLAIN KNOX GELATINE (U.S.P.)

Recent physiological research has confirmed the importance of the phosphocreatine phase in muscle contraction in a group of male subjects, and has shown that energy output can be increased by more than 100% through "concentrated" feedings of plain Knox Gelatine (U.S.P.).

"Proceedings of the Society for Experimental Biology and Medicine", 40:157, 1939.

Knox Gelatine is high in certain amino acids, which are precursors of muscular creatine. Thus, by increasing the phosphocreatine content of the muscle, Knox Gelatine increases its chemical store of potential energy.

The gelatine used in this study was plain Knox Gelatine (U.S.P.) which assays 85% protein and which should not be confused either with inferior grades of gelatine or with sugar-laden dessert powders, for these latter products will not achieve the desired effects. When you desire pure U.S.P. Gelatine, be sure to specify KNOX. Your hospital can get it on order.

EXTRA ENERGY FORMULA

Empty one envelope of Knox Gelatine in a glass three-quarters filled with cold water or fruit juice (or half water and half fruit juice). Let the liquid absorb the gelatine. Then stir briskly and drink immediately before it thickens. Take four times a day for two weeks, then reduce to two envelopes a day. (May be taken before or after meals).

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Let us quote on your special formulae, or may we send you a catalog?

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Continued from page 44

Dr. Robert L. Kimmins, Meridian, aged 72, died June 30 of coronary occlusion.

VIRGINIA

The Medical Society of Virginia will hold its seventieth annual meeting in Richmond October 3, 4 and 5.

The one hundred and forty-third quarterly session of the Southside Virginia Medical Association was held at Piedmont Sanatorium, Burkeville, September 12. The Reception Committee was Dr. J. B. Woodson, Dr. John A. Proffitt and Dr. J. L. Hamner, all of Burkeville. The President is Dr. C. S. Dodd, Petersburg, and the Secretary is Dr. R. L. Raiford, Franklin.

The Augusta County Medical Society has elected the following officers for the coming year: President, Dr. D. E. Watkins, Waynesboro; Vice-Presidents, Dr. John H. Thomas, Greenville; Dr. A. M. McLaughlin, Waynesboro; and Dr. T. R. Rolston, New Hope; Secretary, Dr. J. E. Cox, Waynesboro; Treasurer, Dr. J. E. Womack, Staunton.

The Fauquier County Medical Society has elected the following officers for the coming year: President, Dr. Stewart McBryde, Manassas; Vice-Presidents, Dr. Frank Folk, Warrenton, and Dr. J. R. Allen, Marshall; Secretary-Treasurer, Dr. William R. Pretlow, Warrenton.

Dr. Richard W. Fowlkes, Richmond, has been appointed Associate Professor of Dermatology at the Medical College of Virginia.

Dr. Patrick H. Drewry, formerly of White Plains, New York, has been appointed Assistant Professor of Neuropsychiatry at the

Continued on page 48

Classified Advertisements

RATES for insertion in the Classified Column are as follows: $2.00 minimum, which includes the first 50 words; for each word in addition to the original 50 words, the charge is 3c.

HOSPITAL FOR SALE—Hospital building and equipment located at Sparta, Tennessee. Building has 15 rooms with 11 beds and a standard equipped operating room. This is the only hospital in White County, Tennessee. For information write G. G. Zahn, Liquidator, Federal Deposit Insurance Corporation, care Bank of Donelson, Donelson, Tennessee.

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Vi-Syneral contains Vitamins A, B_1, B_2 (G), C, D, E, fortified with eight essential minerals . . . the original Funk-Dubin multiple vitamin-mineral concentrate.

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MYCOFAN—leaves no greasy or visible coating.

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Will be pleased with the high purity of "PURITAN MAID" CYCLOPROPANE, the excellent results obtained from its use, and the economies effected in the cost of anesthesia. We sincerely urge and invite comparison of our product with any other brand.

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While Cyclopropane itself is a low-pressure gas, it is used often on gas machines opposite high-pressure gas cylinders. The cylinders in which it is marketed, for this and other reasons, should be just as strong as the rest of the system. Don't be misled into the use of cheap light-weight cylinders for this important gas. Consult your insurance engineer and be safe. We use as strong cylinders for Cyclopropane as for any other gas.

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PURITAN MAID
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Carbon Dioxid
Helium

Equipment for the Administration of Helium Gas Mixtures: also Apparatus for the Subcutaneous Injection of Oxygen.

Manufacturers and Distributors—Oxygen Tents, Nasal Catheter Units, Bedside Inhaling Outfits, Anesthetic Gas Machines, Resuscitators and Inhalators, Soda Lime.

Continued from page 46

Medical College of Virginia. He is now doing special work in neuropsychiatry in England.

Dr. W. Hughes Evans, Richmond, announces his association with Dr. H. Hudnall Ware, Jr., for the practice of obstetrics and gynecology.

Dr. William P. McGuire, Winchester, announces his association with his father, Dr. Hunter H. McGuire, limiting his practice to diseases of the eye.

Dr. J. Gordon Rennie, Bedford, is engaged in the practice of general surgery at the John Russell Hospital, having recently come from the St. Luke's Hospital in Bluefield, West Virginia.

Dr. W. H. Copley has located at 1616 Hull Street, Richmond, for the practice of medicine, having recently completed his internship at Johnston-Willis Hospital.

Dr. Joseph S. DeJarnette, Staunton, was recently honored at a luncheon and special meeting for his completion of fifty years on the hospital staff of the Western State Hospital.

Dr. Isaac A. Bigger, Richmond, was elected Treasurer of the American Association of Thoracic Surgery at its recent annual meeting in Los Angeles.

Dr. Claudio R. Arce, Newport News, and Miss Louise Henrietta Berger, Richmond, were married June 14.

Dr. Daniel Sumner Ellis, Richmond, and Miss Eloise Goodman, Newport News, were married June 24.

Dr. John D. Hamner, Jr., and Miss Evelyn Shepherd, both of Richmond, were married June 24.

DEATHS

Dr. Lawrence Taylor Price, Richmond, aged 58, died August 15 of a heart attack.

Dr. James Beverly DeShazo, Ridgeway, aged 70, died July 31.

Dr. Thomas Henry Wilkins, Portsmouth, aged 62, died June 29.

WEST VIRGINIA

Dr. Harvey A. Smith, Wheeling, has been appointed Health Officer of Wheeling and Ohio County.

Dr. John B. Hozier, of the United States Public Health Service, is acting as Director of the West Virginia State Department of Health at Charleston in the absence of Dr. Chas. N. Scott, who will spend a year at Johns Hopkins University.

Dr. Percy Ryland Fox, McComas, and Miss Nina Cornelia Kelly, Bristol, Virginia, were married August 5.

Dr. Robert Glenn Thompson, Three Churches, and Miss Marian Brownlee Hayes, Rock Hill, South Carolina, were married June 29.

Dr. Lawrence H. Mills, Clarksburg, and Miss Mildred Gertrude Young, New Martinsville, were married July 7.

DEATHS

Dr. Joseph Robinson Jones, Charleston, aged 44, died May 26 of acute dilatation of the heart.

Dr. W. B. Stewart, Georgetown, aged 76, died May 29 of intestinal obstruction.

Dr. Joseph Kins Rowland, Flat Top, aged 40, died May 19 of acute encephalitis.

Dr. Ira E. Hall, Morgantown, aged 80, died May 25 of uremia and myocarditis.

Dr. E. W. Hoylman, Secondcreek, aged 64, died June 22 of abscess of the gallbladder and uremia.

Dr. J. Randolph McCutcheon, South Charleston, aged 49, died July 28 of a heart attack.

SCABIES TREATMENT

Tested in 1213 Cases*

CLEAN, PLEASANT ODOR
NON-IRRITATING
RAPIDLY EFFECTIVE

If you would like to give it a test, send 20c to cover handling and we will mail enough for one adult treatment.

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OF THE URINARY TRACT

Most frequent pathological "gangsters" of the urinary tract are the B. coli. Probably the most widely used "G-U gang buster" in colon bacillus urinary tract infections is—methenamine. Clendening finds that **with the urine rendered acid,** methenamine will liberate sufficient formaldehyde to destroy all organisms of a certain type—particularly the B. coli. He recommends acid sodium phosphate as an acidifier. (Methods of Treatment.)

URO-PHOSPHATE Tablets

Acidifier and Antiseptic in One

URO-PHOSPHATE Tablets contain methenamine **plus** acid sodium phosphate—of an extraordinary purity—effecting acidification for immediate and effective "fumigation" of the urinary tract.

Advantages—Only one product to take—no need for litmus tests—complete conversion of methenamine to formaldehyde assured—relatively safe in large doses.

Issued only in hermetically sealed bottles of 100 tablets.

Prescribe URO-PHOSPHATE Tablets in pyelitis (adults and children), cystitis, pyelonephritis and other B. coli infections of the urinary tract; before and after instrumentation. Patients will be grateful for marked relief, decrease in frequency, burning and pain of micturation, its healing tendencies.

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10 and 50 cc. brown bottles in light-proof cartons. Not less than 60,000 vitamin A units, 8,500 vitamin D units (U.S.P.) per gram. 100 times cod liver oil* in vitamins A and D.

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Especially convenient when prescribing vitamins A and D for older children and adults. As pregnancy and lactation increase the need for vitamin D but may be accompanied by aversion to large amounts of fats, Mead's Capsules of Oleum Percomorphum offer maximum vitamin content without overtaxing the digestive system. 25 and 100 10-drop soluble gelatin capsules in cardboard box. Not less than 13,300 vitamin A units, 1,850 vitamin D units (U.S.P.) per capsule.

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Uses: For the prevention and treatment of rickets, tetany, and selected cases of osteomalacia; to prevent poor dentition due to vitamin D deficiency; for pregnant and lactating women; to aid in the control of calcium-phosphorus metabolism; to promote growth in infants and children; to aid in building general resistance lowered by vitamin A deficiency; for invalids, convalescents, and persons on restricted diets; for the prevention and treatment of vitamin A deficiency states including xerophthalmia; and wherever cod liver oil is indicated.

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1 oz. of Pablum contains 221 mg. Ca, 8.5 mg. Fe—So absorptive is Pablum that when mixed to the consistency of ordinary hot cooked cereals it holds 7 times its weight in milk — before being served with milk or cream. Hence an ounce serving of Pablum thus mixed with milk adds at least .53 Gm. calcium to the diet.

	Mg. per Oz.	
	Iron	Calcium
PABLUM	8.5	221.0
Beets	0.67	6.8
Carrots	0.17	13.1
Peas	0.50	8.0
Spinach	1.13	21.8
String Beans	0.27	14.2
Tomatoes	0.12	3.1

Peas
1/17 as much Fe,
1/27 as much Ca
as PABLUM

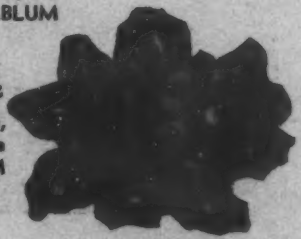
Tomatoes
1/70 as much Fe,
1/71 as much Ca
as PABLUM

Carrots
1/50 as much Fe,
1/17 as much Ca
as PABLUM

NOT only does Pablum have a higher iron and calcium content than vegetables but, most important, clinical studies of children have demonstrated that in Pablum these minerals are in available form. Investigations by Stearns and Stinger, Schlutz, and Cowgill show that even such an iron-rich vegetable as spinach did not increase iron storage in the body, in fact, caused a loss in some instances. A factor responsible for this difference may be the higher content of *soluble* iron in Pablum—7.8 mg. per oz. Then, too, the water in which Pablum is cooked (by a patented process) is dried with it, whereas the cooking water of vegetables is usually discarded, with its valuable content of minerals and vitamins. Stearns reports difficulty in feeding spinach in sufficient quantities to affect the iron balance of children. Spinach and other highly flavored vegetables are often difficult to feed. Pablum, on the other hand, is a palatable cereal that can be fed as early as the third month, and for older children it can be varied in dozens of appetizing dishes. Recipes and samples available on request of physicians.

String Beans
1/31 as much Fe,
1/15 as much Ca
as PABLUM

Beets
1/12 as much Fe,
1/32 as much Ca
as PABLUM



Spinach
1/12 as much Fe,
1/10 as much Ca
as PABLUM

Pablum consists of wheatmeal (farina), oatmeal, wheat embryo, cornmeal, beef bone, brewers yeast, alfalfa leaf, sodium chloride and reduced iron

MEAD JOHNSON & COMPANY
EVANSVILLE, INDIANA, U.S.A.

AN ANTICONVULSANT FOR THE TREATMENT OF EPILEPSY

KAPSEALS DILANTIN SODIUM*

DILANTIN SODIUM (sodium 5,5-diphenylhydantoinate), an anticonvulsant with little or no hypnotic effect, is supplied for the treatment of epileptics not responsive to other medication. Extensive clinical use indicates that Dilantin Sodium will prevent, or greatly decrease the frequency and severity of, convulsive seizures in a majority of epileptics. However, since the significance of observed reactions to Dilantin Sodium is not fully established, patients receiving the drug should be closely observed.

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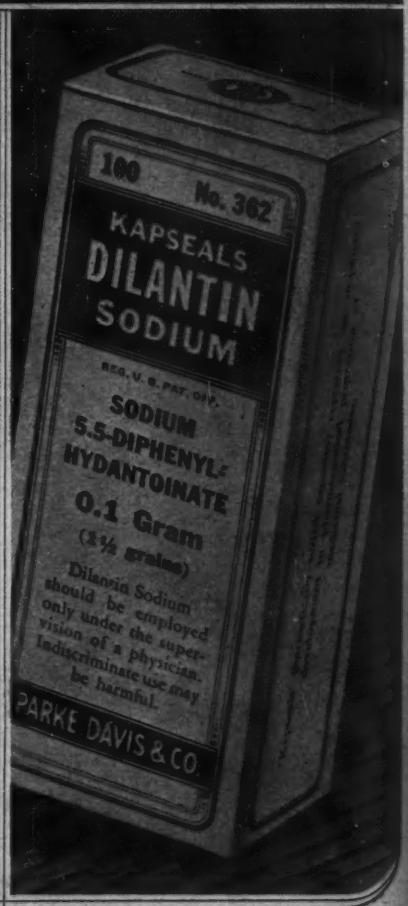
Dilantin Sodium is accepted by the Council on Pharmacy and Chemistry of the American Medical Association for inclusion in New and Nonofficial Remedies.



*** The name 'Dilantin' Sodium designates the sodium salt of diphenyl hydantoin. 'Dilantin' Sodium was formerly known as 'Dilantin,' a term now designating the basic substance, diphenyl hydantoin. Dilantin Sodium is available as 0.1 Gram (1½-grains) and 0.03 Gram (½-grain) Kapseals, in bottles of 100, 500 and 1000.**

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